M

A MANUAL

OF

PATHOLOGY

BY

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PREFACE TO THE THIRD EDITION

THE increasing favor shown toward this manual indicates that it must have fulfilled to a great extent the purpose as first stated, which was that it should present briefly, but yet clearly, those points which appeared to be essential to the understanding of the subject of pathology.

In the second edition many changes were made both in the arrangement and in the text. This present edition, the third, although not showing much rearrangement, has been enlarged quite markedly. New material has been added, much of the old revised, and other parts completely rewritten. This is particularly the case concerning the chapter on the Blood, which is entirely new.

Many of the old illustrations have been replaced by new and more have been added so that the total number is much increased.

It is hoped that this edition will be received as cordially as the previous two.

GUTHRIE MCCONNELL.

PHILADELPHIA, PA.,
September 1915.

PREFACE

The purpose of this volume is not that it shall attempt to take the place of the more voluminous text-books on pathology, but that it shall enable the student especially to rapidly acquire the salient points of a subject. To this end the author has sought brevity, but has tried at the same time not to sacrifice clearness in the exposition of the material.

If the student finds that this manual fulfils the above conditions the author will have accomplished his purpose.

G. McC.

ST. LOUIS, MO.

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A MANUAL OF PATHOLOGY

PART I—GENERAL PATHOLOGY

CHAPTER I

PATHOLOGY

"**Pathology** is that subdivision of biology which has for its object the study of life in its abnormal relations." It is the science that treats of disease in all its aspects.

By "disease" is meant any condition in which there is a variation from the normal aspect of the organism; it may be either a structural or a functional deviation.

Pathology also may be subdivided into two sections: one known as *morbid anatomy* and *histology*, in which the lesions are structural. The other, *morbid physiology*, in which the changes are functional.

The main heading may be again subdivided into *general pathology*, that deals with abnormal processes common to the entire organism, such as inflammation, fever, etc., and *special pathology*, that includes the changes within special organs.

Under **etiology** are considered the conditions giving rise to disease. They may be either *predisposing* or *exciting*.

Predisposing causes are those that in any way lower the vitality of the individual and thus render him more susceptible; such as bad hygienic surroundings, poor food, bad air, noxious gases, fatigue, extremes of temperature, drugs, injury, pre-existing disease.

Exciting causes include mechanical forces, sudden extremes of heat and cold, electricity, poisons, parasites, and also certain mechanical abnormalities, such as defects in the heart-valves.

Although the causes are divided into these two classes, a predisposing cause if acting with great severity may readily excite disease.

The individual may be the seat of two diseases, one acting primarily and another following secondarily.

The latter may be either the direct result of the primary or may have nothing whatever to do with it. Infection of the lung by the tubercle bacillus gives rise to phthisis; later on there may be involvement of pleura or of intestines, or a person suffering from chronic nephritis will often die from a secondary pneumonia.

Traumatism may cause disturbances of function more or less marked according to the extent, severity, rapidity, and duration of its action.

If it takes the form of constant pressure, there will be malnutrition and atrophy of the part on account of the interference with the blood-supply. If the pressure is intermittent, hyperemia may occur and hypertrophy take place.

When the force is sudden the lesions vary according to the instrument used. If sharp, there are lacerations; if dull, contusions.

According to the locality, there may be fractures and concussion. In all these injuries there is greater or less destruction of tissue, followed by the phenomena of inflammation, with either recovery or death.

Temperature.—Following the local action of extreme *heat* a condition known as a *burn* results, in which there is relaxation of the blood-vessels, exudation of serum, and possibly of blood. The extent of the injury to the tissues depends on the degree of heat and its time of action. According to the extent, burns may be divided into four classes: (1) Hyperemia of the exposed surface; (2) extravasation of serum and liquefaction of certain cells, thus forming vesicles; (3) coagulation of the cellular protoplasm with resulting necrosis and extension into the deeper tissues; (4) charring of the tissues and extensive, deep involvement.

Death may result from burns, either immediately from shock or later from exhaustion, from a perforating ulcer of

the duodenum, or from toxic substances formed either within the body or absorbed from the skin. There may be marked alterations within the blood and their action may prevent the kidneys from carrying on their functions.

The cause of the duodenal ulcer is not clear, but may depend upon thrombosis of some small vessel and subsequent digestion by the gastric juice. As a rule, a burn, even of the first degree, will prove fatal if it involves one-third the surface of the body.

If the exposure has been general, the result will vary according to the cause, whether steam, dry air, or sun, etc. Exposure to dry air or sun may cause heatstroke or heat exhaustion. In the first there occur symptoms of heart failure, dyspnea, and coma, if severe. Usually the pulse is full and rapid, face flushed, very high temperature, dry skin, labored breathing, unconsciousness, and muscular relaxation. In heat exhaustion the skin is moist, cool, pale, pulse small and soft, unconsciousness unusual, and temperature may be subnormal.

Extreme cold will bring about conditions very similar to those resulting from heat, and will have various symptoms, according to whether the effects have been superficial or deep. In the former the tissue may completely recover, but in the latter the blood-vessels may be involved and gangrene follow.

The primary effect of cold is to bring about a contraction of the superficial blood-vessels. This, however, gives way to a paralytic dilatation, on account of which more blood enters the chilled part and the entire body will be affected.

If the tissue should freeze during the stage of contraction, the part would appear pale; if during that of dilatation, it would be swollen and dusky in color.

Electricity causes destruction of tissue either by the heat generated or by the resistance of the body to its passage.

Death may result instantly from disturbance of the nervous system or there may be extensive and destructive burns. Sometimes there is involvement of internal organs.

X-rays when applied too closely or for too great a length of time occasionally give rise to a dermatitis or even to burns

of the first, second, or third degrees. As a sequel to the dermatitis, squamous-celled carcinoma has quite frequently developed and gone on to a fatal termination.

Barometric pressure may cause disturbances if it be either greatly increased, as in deep-sea divers or caisson-workers, or diminished, as in mountain-climbers and in persons ascending in balloons. In the latter the blood shows an increase in the number of red corpuscles, in their specific gravity, and in their hemoglobin content.

Season also has a distinct effect upon disease; pneumonia and bronchitis being most common in winter, typhoid fever and malaria in spring, yellow fever and enteric disorders in the summer. In cold weather certain diseases become more frequent on account of the crowding of the people.

Intoxication.—A *poison* is a substance which when introduced into the living body in a relatively small amount will disturb the structure or functional activity. These substances may be formed within the body through faulty metabolism and give rise to *endogenous* or auto-intoxication. They may result also from faulty elimination, irregular absorption, incomplete chemical transportation, or excessive glandular secretion. They may be introduced from without, *exogenous* intoxication. The exogenous may be (1) *immediate* and *indiscriminate* in their action or they may be (2) *remote* and *selective.*

1. The first group includes the *caustics* and *irritants*. Their effects are the more marked the greater the concentration, and may be purely local. The poison may, however, be absorbed and give rise to remote effects. In this class belong the salts of the heavy metals, a few vegetable substances, and some animal products.

The effects may vary from a slight reddening to marked necrosis and sloughing. They are brought about by abstracting the water from the tissue, by coagulating the albumins, and forming definite compounds with the elements. The effect depends on various conditions both of the individual and of the poison. If a patient has been addicted to the use of a drug, a dose fatal to others may cause in him very slight disturbance, a condition known as tolerance, and not similar

to immunity. Sometimes a very large dose may cause vomiting, and the poison is in that way removed.

2. Many of the first group come secondarily into this class by being absorbed and taken up into the blood. They may unite with the hemoglobin or they may bring about *hemolysis*, a destruction of the red corpuscles.

When the poison combines with the hemoglobin, forming methemoglobin, the union is so close that the oxygen can no longer be taken up and supplied to the tissue. Death then results from a general asphyxia. Instead of death, cyanosis may develop, this commonly resulting from the use of coal-tar products.

Strychnin is selective in its action, in that it stimulates the respiratory centers and the motor nerves. Bromids depress them.

Foreign bodies that are not living may cause disease by mechanically interfering with the functions of the body. The most important causes of disease are, however, *bacteria*, the lowest forms of vegetable life. They are almost ubiquitous and give rise to many disturbances of function. It is not, however, always possible to prove the relationship between bacteria and disease. Koch has advanced four laws. They are: (1) The bacteria must be found in the diseased individual; (2) they must be capable of cultivation upon media outside the body; (3) pure cultures introduced into a healthy animal must produce the disease in the animal; (4) the bacteria must be recovered from the inoculated animal.

Diseases caused by bacteria are capable of transmission from person to person and are generally termed *infectious*. They may gain entrance into the body through abrasions of the skin and mucous membranes, through the air or by means of the digestive tract, through the genito-urinary tract, or they may be transferred from the maternal to the fetal blood in the uterus.

Animal parasites may frequently be the cause of disease. To this class belong the various intestinal worms and certain blood organisms, as the plasmodium of malaria, the filaria, the trypanosomes, etc.

CHAPTER II

DEFECTS OF DEVELOPMENT

A malformation is any deviation from the normal embryonal development. This may be the result either of some disturbance taking place in the self-developing power of the embryo, or else due to some influence directly concerned with the maternal structures. The causes may be either internal, existing in the embryo itself, or external, those acting from without.

If the development is only slightly imperfect the condition is called a *malformation;* if marked, it is a *monster*. The defect may occur within an individual or there may be two or more united individuals, the latter being either double or triple monsters.

To have any serious malformation taking place, the causes must have begun to exert themselves very early in embryonal life. In such cases the lesions will generally be of such a nature that extra-uterine existence is impossible. It is probable that such take place before the third month.

The malformations brought about by external causes usually occur during the later period of fetal development. As a rule, they are not of sufficient gravity to prevent the child from living.

Some of the departures from normal occur in different cases, but with about the same appearances; these are spoken of as *typical* and are due generally to some internal cause, harelip being such an example. If the malformation is entirely unusual it is *atypical*, and results from external factors.

If the variation is one that is present in either parent it is spoken of as an inherited abnormality, as in the frequent occurrence of extra fingers or teeth in successive genera-

tions; is also seen in the way in which certain diseases are transmitted from parent to offspring.

If the abnormality passes over one or two generations before reappearing, the condition is known as *atavism*.

Varieties of Congenital Malformation.—The chief single forms of deviation are divided as follows:

1. *Aplasia*, or complete failure of development, which may be either general or local. If general, *abortion* usually results and the embryo is cast off. It may, however, be infiltrated with lime salts, forming a *lithopedion*. Examples of the local form are absence of parts of the body, as fingers, toes, and internal organs. This condition may prevent life, as in the absence of the brain or heart.

2. *Hypoplasia* is the failure of parts of the body to reach their full development, as in small size of limbs or of the brain. It is seen in cases where one kidney may be very large and the other very small.

3. Incomplete union along the line of closure of the fetal arches may be anterior, posterior, or lateral, such as extrusion of viscera, spina bifida, and harelip.

4. There may be an abnormal union of parts, as of the lower extremities.

5. Occasionally there is a duplication of parts, particularly of the digits; sometimes of the internal organs, as the spleen and pancreas.

6. Abnormal location of viscera. In these cases all the single organs are transposed, the heart and spleen on the right, the liver on the left side.

7. Obstruction of the external openings, mouth, anus, vagina, etc.

8. Persistent misplaced fetal structure, which may eventually give rise to neoplastic formations, usually cystic.

9. Anomalies of sex—hermaphroditism, which may be either true or false. In the early stages the embryo is bisexual, but finally one set of organs undergoes a perfect development, with slight traces only of the subsidiary organs. In the true form both sets of organs would be present, well devel-

oped. This condition is so rare that it is said not to exist, one case only having been reported.

In false hermaphroditism the malformation depends upon abnormalities of the external genitalia.

Double Monsters.—In these there is a duplication of the whole body, the halves being attached to each other, or a duplication of either caudal or cephalic end. Such monsters are always of the same sex and are usually joined at corresponding parts, as head, thorax, or sacrum. They arise from a single ovum and blastodermic vesicle, and the cause that determines their formation must exert its influence at the earliest stage of development, probably during the formation of the primitive streak and medullary groove.

They may result from:

1. Two embryonic areas arising within a single blastodermic vesicle and continuing to grow.

2. Two primitive streaks and two medullary folds arising within a single embryonic area and either remaining separate or merging.

3. A single primitive streak with either partial or complete doubling of the medullary groove.

4. The duplication may take place late in the development and affect only single parts.

The first three cause abnormalities along the main axis of the body; in the fourth, the variations lie to one side.

Twins and triplets in a way belong to the class of monstrosities, as they are a reversion to the lower types, in which multiple births are common.

The twins may be equally developed and of the same size, or one may be larger and more advanced. They will in the first case usually live; in the second they sometimes continue to exist.

The varieties of double monsters are named by adding the word "pagus" (from *pag*, meaning "to fasten") to the name of the part of the body by which they are attached, as xiphopagi, when joined by the xiphoid cartilage; cephalo-pagus if by the heads.

These monstrosities may or may not live, according to

the development of the internal organs. In many cases each individual has had well-developed and separate organs and the two have lived for many years.

Sometimes one of the twins may take up the nutrition at the expense of the other, with subsequent increase in size. The larger of the two is called an *autosite*, and the other a *parasite*. The latter is generally imperfectly developed.

The abnormalities of the various important organs will be considered in their respective chapters in Part II.

CHAPTER III

DISORDERS OF METABOLISM

By **metabolism** is meant those physiologic processes brought about in living tissue by means of which the individual is able to form new tissue and reintegrate the old. Under this head comes the rejection of those substances that are unfit for use in the bodily economy.

In order that the functions of the body be carried on in a normal manner it is necessary that the amount taken up by the cells must balance the output. The metabolic equilibrium must be maintained. To carry on the work it is not sufficient that new material be taken in, more is required. These new substances must be assimilated by the body, broken down into various parts, and the waste portions excreted. Disturbances of any of these above factors, constituting metabolism, may give rise to diseased conditions of varying importance.

When the tissues are unable to carry on these molecular exchanges a pathologic condition exists. This may be either functional or structural, the latter generally being secondary to the former.

Metabolism may be divided into two classes, according to whether simple substances are built up into complex, or the complex broken down into the simple. The building-up or constructive variety is called *anabolic metabolism;* the breaking down or destructive, *catabolic metabolism.*

By means of catabolism the "end products," those substances not required by the body, are formed, such as urea, water, etc. Anabolism is concerned in the rearranging of molecules so as to render them suitable for food.

A food is a substance that will form new or reintegrate old tissues. It may be either in excess or in diminution, or may vary in quality, the amount required depending upon the activity of the individual.

The assimilation of food depends upon the presence within the gastro-intestinal tract of certain digestive ferments, which may vary greatly in quantity.

The *protein* substances are acted upon by the pepsin in the stomach and the trypsin from the pancreas. Pepsin acts in an acid medium; trypsin in an alkaline. The necessary acid in the stomach is the hydrochloric. Changes from the normal amount of pepsin are unusual, but there may be great variations as far as the acid is concerned. It may be increased, *hyperchlorhydria;* diminished, *hypochlorhydria;* or absent, *achlorhydria.* If absent or much diminished, the food, not being properly digested, will undergo fermentation. If there be any obstruction at the pylorus the stomach will tend to dilate.

The *carbohydrates* are acted upon first in the mouth by the salivary ferment, *ptyalin;* then in the intestines by *amylopsin*, a ferment derived from the pancreas.

The *fats* are acted upon by *steapsin*, a pancreatic ferment, and by the bile.

The condition of the individual depends upon the assimilation of the food, which may be abnormal in quantity or quality.

If the quantity taken up by the individual is diminished, either by lack in amount or by being deflected from its proper channels, certain pathologic conditions will result. These may be *emaciation* or *starvation*, in which case the body weight diminishes, the temperature falls, and the energies all fail. At first the reserved food is called upon. The circulating proteins are first used up, then the glycogen, and afterward the fats and the muscles. The heart and the central nervous system are the last structures to be involved. The organs become smaller, the excretions and secretions are gradually suspended. In the blood the leukocytes become much fewer, although the red cells appear in normal number. This is probably due to the loss of the blood-serum. Death takes place slowly, either from exhaustion, disorders of metabolism, or by terminal infections.

In **marasmus,** a term applied to babies and old people, the wasting away takes place more slowly than in starvation.

In it the trouble is very frequently not due to lack in quantity of food, but to improper assimilation.

If during the course of a definite disease these symptoms of slow starvation appear, the condition is called **cachexia.** In it there is a peculiar yellowish color of the skin and also a marked anemia. It is probably due to the formation of toxic substances, many resembling ferments, which produce injurious effects upon the normal tissues of the body.

Rickets, or **rachitis,** is a condition of childhood that is indicated by structural changes of the bones, particularly those of the pelvis and of the lower extremities. It is characterized by an excessive formation of cartilaginous bone followed by a deficient deposit of bony salts. Such bones are not perfectly rigid and tend to show more or less deformities on that account. Eventually enough salts may be deposited to render the bone rigid, but it will retain its irregular structure. In these children dentition is late and the teeth readily undergo carious changes.

If larger amounts of food are taken than are necessary for the bodily requirements, the excess will be carried through the intestines unacted upon. It may result in an excessive formation of fatty tissue, giving rise to the condition known as *obesity* or *polysarcia.* This is due either to the excessive absorption of food, either fats or substances, like carbohydrates, whose catabolism yields fats, or to inadequate combustion of the fats so acquired. In some cases both factors may play a part.

In **asphyxia** there is a lack in the amount of oxygen and an increase in the carbon dioxid. In this process there is first a period of increase in the inspiratory efforts, then in the expiratory, and finally exhaustion. After death the heart, particularly the right side, is found to be distended with blood.

Dyspnea is a slight lack of oxygen, sufficient to stimulate but not to depress the respiratory centers. *Cyanosis,* a bluish color of the skin, particularly of the face, then appearing. *Apnea* is a condition in which there is a period when no respiratory action takes place.

Abnormalities in the secretions of the organs may cause

marked disturbance. The secretions may be either *internal* or *external*. The external pass directly from the glands by means of ducts. The internal pass slowly into the blood, which carries them to all parts of the body. In addition to the actions of the better known internal secretions are others, called *hormones*, whose functions appear to be to stimulate to full activity other digestive glands, even those situated at a distance.

The **thyroid secretion,** when lessened or absent, gives rise to the condition known as *myxedema*. In this the skin becomes much swollen and firm, particularly in the region of the face. The skin will not pit on pressure nor are the dependent portions affected. The hair frequently falls out, the voice undergoes changes, and there are commonly decided disturbances of mentality. If sheep's thyroid gland is given in such cases there is frequently a decided improvement.

Cretinism is a very similar but more severe condition resulting from disease of the thyroid during intra-uterine life or in early childhood, usually appearing during the first year. The child does not develop, remains a dwarf, there is more or less complete loss of mind, the lips are very thick, tongue large, and the abdomen very pendulous. Frequently several members of a family are found to be suffering from it. The state is also occasionally markedly hereditary.

If the thyroid secretion be increased, there may result *exophthalmic goiter*, or Basedow's disease. It is characterized by enlargement of the thyroid gland, paroxysms of palpitation of the heart, bulging of the eyes, and nervous excitement. In this the administration of sheep's thyroid increases the symptoms.

The relationship between the thyroid gland and general disease is not clearly understood. There appears to be distinct bearing upon the nervous system and also upon the metabolic processes taking place within the body. The active principle seems to be "thyroidin," a substance that contains nearly 10 per cent. of iodin.

The *parathyroids* are several small pea-like bodies situated close to the thyroid, and histologically resemble the unde-

veloped thyroid. Their removal is followed by the condition called *tetany*, which manifests itself by exophthalmos, rapid respiration, and painful tonic muscular spasms, most marked in the hands and feet. These symptoms may be due to a loss of ability to neutralize toxins. Relief from them has been obtained by the intravascular use of a soluble lime salt.

The secretion of the **adrenals** is obtained from the medullary portion which is developed from the same source as the sympathetic ganglia. It is evidently derived from the chromaffin cells, so-called on account of their affinity for the chrome salts. Wherever those cells are present the active principle can be procured, the greatest collection being in the adrenal. This secretion is evidently of marked importance, as disease of or removal of those bodies causes severe disturbances in the individual. If completely removed, collapse and death occur within a few hours. When the breaking down has taken place slowly, a condition known as *Addison's disease* results. In it there is an increasing weakness, accompanied by anemia, emaciation, and a peculiar bronzing of the skin and mucous membrane of the mouth.

Whether or not it has a relation to the pigmentation of the skin and to the cachexia is not settled, but it is probably the result of oxidation by the secretion.

The action of the adrenal secretion seems to be more upon the vasomotor system. When applied locally the vessels will contract, and if injected into the circulation will cause a rise in blood-pressure. This is due to the contraction of the arterioles.

The secretion of the **pituitary body** seems to bear definitely upon the nutrition of the tissues. When diseased the condition of *acromegaly* is generally present. In it there is a marked enlargement of the bones of the face and of the extremities. The enlargement is due to an actual hypertrophy of the parts involved. Accompanying this there is usually some interference with speech, and the memory is slightly affected.

In the *pancreas*, besides the three external secretions, there is also an internal one. It seems to be chiefly concerned in carbohydrate metabolism; it is a glycolytic ferment.

Diabetes is a disease in which the carbohydrates are not properly assimilated, and is characterized by the persistent appearance of sugar, chiefly as dextrose, in the urine. In this way it differs from alimentary glycosuria, in which the sugar appears transitorily. The abnormal condition of the urine in diabetes is the direct result of an altered composition of the blood, which in turn is caused by changes in metabolism. Examination of the blood in diabetes always shows an increase of sugar above the normal of 0.1 per cent., a condition known as *hyperglycemia.* This increase of sugar may be due to any of the following conditions: (1) Impairment of the glycogenic function of the liver and muscles, caused by the cells being unable to store dextrose as glycogen; (2) impairment of the power of the muscles and other tissues to utilize dextrose; (3) overproduction of dextrose from glycogen, protein, or fat.

As the pathology of many cases of diabetes is so uncertain or obscure, it is difficult to classify them according to the pathologic conditions, but from the point of view of metabolism diabetic patients may be divided into two great groups: (1) Cases of mild diabetes, in which the glycosuria ceases as soon as the carbohydrates in their food have been sufficiently reduced. In most of these cases the glycosuria depends entirely upon the quantity or kind of carbohydrate in the food. (2) Cases of severe diabetes, in which the glycosuria does not cease as soon as their diet is freed from carbohydrates. They must, therefore, excrete dextrose derived from protein or fat as well as from carbohydrates.

Mild Diabetes.—This group may be divided into four varieties, according to the pathologic condition which causes the change in metabolism:

1. *Neurogenous diabetes* is caused by the action of the nervous system upon the liver. It has been shown that puncture at the tip of the calamus scriptorius in the fourth ventricle is followed generally by hyperglycemia and glycosuria. At present it would appear that this hyperglycemia following puncture is due to dextrose produced from hepatic glycogen, and that this conversion is an overproduction because it takes place irrespectively of the needs of the tissues. A similar condition may

occur in the course of tumors or diseases of the brain, as well as in fractures at the base of the skull.

2. *Hepatogenous Diabetes.*—In view of the importance of the glycogenic function of the liver in preventing hyperglycemia after carbohydrate meals, it is not surprising that parenchymatous disease of the liver may produce glycosuria.

3. *Lipogenous Diabetes.*—Patients suffering from any variety of mild diabetes may be fat, but there appear to be cases in which the diabetes has some direct connection, at any rate in point of time, with obesity. It has been suggested that there are patients who have lost the power of assimilating carbohydrates properly, but who do not have glycosuria as long as they retain the power of converting the excess of carbohydrates into fat. When this power becomes impaired, these patients develop glycosuria.

4. *Pancreatic Diabetes.*—In this variety there is a partial failure of the internal secretion of the pancreas which induces a mild degree of diabetes. Although this form of diabetes is pathologically distinct, clinically there is nothing to distinguish it from the other varieties considered. It has, however, been found that if the lesion progresses sufficiently the diabetes changes from the mild to the severe type, and of no other variety of mild diabetes does this hold true.

Severe Diabetes.—The essential feature in the metabolism of these cases is that they excrete dextrose derived not only from carbohydrate food, but also either from tissue fat or from protein food, or from both sources at the same time. This disturbed metabolism is evidently due to the absence of an internal secretion of the pancreas. Tying the pancreatic duct does not cause glycosuria, but extirpation of the organ gives rise to a glycosuria closely resembling diabetes and terminating fatally.

The structures most intimately concerned are the islands of Langerhans which are most numerous in the tail or splenic end of the gland, and are supposed to regulate the metabolism of sugar. If the lesions involve these structures, then diabetes ensues; if, however, the head end alone is affected, there may be no glycosuria. The common lesion of the islands is primarily

a connective-tissue overgrowth which frequently undergoes a degeneration belonging to the hyaline type. There is the formation of a homogeneous substance that stains with the acid dyes, but does not give the amyloid reaction.

The natural termination of all severe and progressive cases of diabetes is in coma due to the formation of acetone bodies, the mother substance of which is beta-oxybutyric acid. This on oxidation yields aceto-acetic acid, and this in turn, by the loss of CO_2, forms acetone. The main source of these acetone bodies is probably fat and not proteins, but it is quite possible that they do have a double source of origin, and that the relative quantities derived from the two sources will vary with circumstances.

According to the quantity and kind of acetone body excreted on a standard diet containing about 50 to 70 gm. of starch, it is possible to divide severe diabetes into three stages: In the first stage are those which secrete acetone alone, and in quantities which vary from the normal 0.05 to 0.5 gm. a day. Such cases retain considerable power of utilizing carbohydrates. The second stage is marked by the constant appearance of diacetic acid in the urine, and this always takes place when the excretion of acetone is more than about 0.5 gm. a day. Patients in this stage still retain some power of utilizing carbohydrates. The third stage begins when beta-oxybutyric acid is always present in the urine, and this is so when more than about 1 gm. of acetone is excreted in the day. Cases in this stage show little or no power of utilizing carbohydrates.

The coma that results is probably due to changes taking place within the cells of the body and not in the blood, the hypothesis at present being that the coma is due to a change in the reactivity of cells produced by the acidosis.

Uremia is a condition associated with disease of the kidneys and characterized by various clinical manifestations, as drowsiness, stupor, coma, twitchings of the muscles, cramps, convulsions, vomiting, blindness, and frequently death. The cause of this condition is not known. It evidently is not due to an increased amount of urea in the blood, as that substance has been proved to be but feebly toxic and incapable of producing

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the symptoms of uremia. The evidence indicates the presence of poison, either singly or in a group. It may be due to the retention within the body of some substance that normally is excreted; to the abnormal decomposition in the blood or tissues of such a substance, or to the formation of abnormal products. Decomposition of urea may result in the production of ammonium carbamate and ammonium carbonate, and these substances when introduced into the circulation give rise to symptoms resembling those of uremia. Examination, however, of the blood in uremia does not show any excess of ammonia. It has been suggested that the kidney produces an internal secretion, and that uremia is due to some change in quantity or quality of this theoretic substance.

Eclampsia is a condition occurring in pregnant women that clinically seems closely allied to uremia, although it may be present without any albuminuria. When death takes place the liver will show congestion, capillary thrombosis, anemic and hemorrhagic necroses, and thrombosis. The kidney will present a nephritis ranging from a slight parenchymatous degeneration to an acute, intense nephritis. It is claimed by some that eclampsia is due to a deficient oxidizing capacity on the part of the liver which fails to convert protein derivatives into urea. There are others who believe that the toxic substances are probably derived from the fetus or the placenta.

Gout or **podagra,** is a disease in which there is deposited within the joints, in the articular cartilages, uric acid and its compounds. It generally affects the small joints of the hands and feet, particularly the big toes. These salts may be deposited elsewhere, as tophi in the cartilages of the ear and in the meninges. As a result of these deposits the joints may be much deformed. Lesions of other portions of the body are usually present. There is a marked tendency toward the formation of connective tissue in the form of interstitial nephritis and of arteriosclerosis; fatty changes also take place in the heart and liver. Gout usually appears after middle life in those who have lived very well, drunk plenty of wine, and have not taken exercise. It is a chronic disease, but

exhibits periods of acute and painful inflammation lasting several days.

It is probably the outcome of insufficient oxidation, by which the precursors of uric acid and similar bodies are not fully oxidized, and by their accumulation and toxicity set up morbid changes.

The salts concerned are the sodium biurates and quadriurates, uric acid existing in the blood in the form of the latter. The soluble quadriurates circulating in the blood, if in the presence of uric acid and sodium salts in excess, are precipitated as insoluble crystalline biurates.

In **oxaluria** and **phosphaturia** there is an excess of either oxalic acid salts or of phosphates. The presence of oxalic acid is thought by some to be due to the amount present in the vegetable matter consumed, while others think it is the result of deficient oxidation of the carbohydrates. It is of chief importance in the formation of calculi, it being precipitated in the crystalline form mainly when there is an increased amount of calcium in the urine.

The phosphoric acid exists in the form of the phosphates of magnesium, ammonium, and sodium. These may form calculi in the bladder when they occur in excessive amount in an alkaline urine, as they remain in solution if the reaction is acid.

Acetone and *diacetic acid* are often found in the blood and urine in the later stages of diabetes.

The **bile** may vary in amount and consistency and may be prevented from passing into the bowel. The normal amount secreted varies from 500 to 1000 c.c. in a day. It is composed chiefly of water, but contains bile salts, cholesterin, lecithin, fat, and coloring substances. The salts are the glycocholate and the taurocholate of sodium. The important pigments are bilirubin and biliverdin, both of which are derived from the blood. Bilirubin undergoes oxidation to form various other pigments. It resembles hematoidin, and the toxic effects of the retention of bile seem to depend upon its presence, as when the bile is freed from its coloring-matters by filtration it is only one-third as toxic as in its original condition.

The most important function of bile is to increase the activity of the pancreatic ferments. It not only increases the fat-dissolving action of the steapsin, but it dissolves and increases the solubility of soaps, and so renders their absorption more easy. Consequently, if bile is absent from the intestines, but pancreatic juice is still secreted, from one-quarter to one-half of the fat taken in the food is unabsorbed.

Bile is not, as has been supposed, an antiseptic, consequently its absence from the intestinal contents neither increases the number of bacteria nor their fermentative or putrefactive activity.

If there should be any obstruction to the outflow of bile the condition known as **icterus** or **jaundice** follows. This obstruction may result from a catarrhal condition or a stenosis of the bile capillaries, inflammation of the common bile-duct, or of the papilla. It may be due to foreign substances, such as gall-stones, inspissated mucus, round-worms, or tumors within the large duct, or to pressure upon it from without. The jaundice is due to the absorption of the bile into the general circulation by means of the veins or lymphatics. A large amount of it is eliminated by the kidneys, while the excess is deposited within the connective tissues.

As a result of the absorption of the bile the skin is at first yellow, but if the condition continues for some time the pigment oxidizes and becomes greenish in color. This discoloration will be seen in the sclera, the lining of the arterial system, the mucous membranes, and in most secretions and exudations, normal or pathologic. The heart's action is frequently slowed (bradycardia) to 50 or even 20 beats a minute.

The effect upon digestion may be quite marked. There is found an excessive amount of fat in the feces. The stools become very light in color, due to the absence of hydrobilirubin, and may be very offensive on account of the loss of the laxative action of the hepatic secretion and consequent stagnation of the intestinal contents. There may be some interference with the outflow of the pancreatic enzyme, which would have a distinct effect upon the amount of fat present and also upon the color of the feces.

Sometimes there are marked nervous symptoms, probably the result of the presence of the biliary acids and salts in the circulation rather than due to the pigments.

Another form of jaundice is that of hematogenous origin. It occurs when no obstruction to the outflow of bile can be found. Although bile cannot be formed in any other place than in the liver cells, there are cases in which a general yellowish discoloration takes place without any hepatic lesion being present. It occurs in certain infectious diseases, as in yellow fever, malaria, etc., in poisoning by venom and toluolendiamin, and in the newborn in the form of icterus neonatorum. In all these conditions, particularly in the last named, there is a very marked destruction of the erythrocytes. The blood-pigment is changed into bile-pigment and thus stains the tissue. This form may be due to some nervous disturbances that cause a contraction of the circular muscles of the bile-ducts. It may be that there is an increase in the viscosity of the bile on account of the presence of the blood-pigments, and in that way the ready outflow is prevented. It has also been shown that the concentration of the bile is associated with an inflammatory condition of the bile-ducts.

Besides the secretion of bile the liver also forms urea and glycogen, but these two latter bodies are carried off in the blood.

Intestinal disturbances may bring about a condition of putrefaction accompanied by various symptoms of self-intoxication, inasmuch as the feces are made up of the remnants of digestion and of waste products. Their odor is due to the presence of indol and skatol.

The intestinal disturbances are due chiefly to the presence of bacteria and their products. Fermentation may take place in the stomach with the formation of acetic, lactic or butyric acids, or of alcohol. It results from the breaking down of the carbohydrates. In the intestine the proteins may undergo putrefaction and produce amido-acids, or aromatic bodies, as acetone, tyrosin, cresol, skatol, and indol. Ptomains may be formed and give rise to many symptoms. These bodies resemble quite closely many of the vegetable

alkaloids and give rise to symptoms similar to those resulting from the drugs.

As a result of these disturbances *diarrhea* may occur. In this condition the feces are too soft and the bowel movements too numerous. It is an attempt to free the body of the irritating substances and may relieve the patient. The diarrhea may be due to increased rapidity of peristalsis, increased secretion of the intestines, diminished absorption by the large intestine, or disturbances of the controlling nervous mechanism, these depending upon many causes. These may be mechanical, inflammatory, infectious, obstructive, hepatic, and pancreatic.

Constipation, or *coprostasis*, is a condition in which defecation may not be sufficiently frequent, the amount of feces insufficient or abnormally dry and hard. It may be due to deficient motor activity of the colon as a result of weak muscle, deficient reflex activity, inhibition of the motor activity, uncontrolled and irregular motor activity. It may be due also to excessive force required to carry the feces to the pelvic colon. The work to be done by the intestinal musculature is excessive whenever the bulk or the consistence of the feces offers more than a normal degree of resistance, and whenever there is any narrowing of the intestinal lumen.

CHAPTER IV

CIRCULATORY DISORDERS

THE circulation of the blood is maintained chiefly by two forces—the rhythmic contraction of the heart muscle and the elasticity of the arteries. Other factors concerned are the compression of the veins by the muscles and the inspiratory action of the chest.

As these are the chief factors, any abnormality within them will bring about more or less general disturbances of the circulation. To these may be added alteration in the quantity or quality of the blood itself. According as to whether the effect is more marked in the systemic or in the pulmonary circulations the disturbances are more or less widely distributed.

The circulatory disorders may be *cardiac* in origin and either the result of *muscular* or *valvular* lesions. If muscular, there may be an *excessive* or, what is more common, a *diminished* action.

The *excessive* form is seldom lasting, but while present causes a rise of blood-pressure, an increased amount of blood within the vessels in the part involved, and an increase in the rate of flow. If the overaction should be long continued, as a result of hard work or by constant stimulation, there would be hypertrophy of the left ventricle.

Diminished activity is more common and more important than the above. It may be brought about in many ways. It may be the sequel of a heart muscle weakened by the infectious fevers or other diseases, by poisons, by lack of nourishment caused by anemia, or by a blocking of the coronary arteries. It may be the result of nervous disturbances with no apparent lesion of the muscle, or it may be the result of some valvular disorder.

Sometimes it results from pressure from the outside—that exerted by collections of fluid in the pericardium, in the pleuræ, or by tumors or adhesions.

As a result of the weakened circulation there is an accumulation of blood in the venous circulation. If the failure is of the left ventricle, there will be a damming back of the blood in the left auricle and in the pulmonary circulation. If the right heart remains capable, the engorgement will go no further, but when it fails the right auricle becomes distended and a condition of general passive congestion ensues.

In all cases there is a decrease of arterial and an increase of venous pressure.

When the heart's action has become much weakened it will be found that the blood tends to gravitate to the more dependent portions, giving rise to *hypostatic congestion.* It occurs in the late stages of severe fevers and when death has taken place very slowly. The dependent tissues will become livid through the accumulation of blood, edematous from the escape of fluid from the blood-vessels, and sometimes bed-sores may result. A frequent occurrence is a collection of blood within the lungs, a condition known as hypostatic pneumonia.

The changes within the *arteries* may be either *organic* or *nervous* (vasomotor). Their elasticity may be diminished, and their caliber increased or diminished. The alteration in caliber may be due to changes within the tissues or to disturbances of the vasomotor control.

If there is a paralysis of the controlling nerves, the vessels dilate and hyperemia results. On the other hand, stimulation will cause contraction and subsequent anemia. When sufficiently marked, there will be an increase in the blood-pressure, interference with the heart's action, and venous congestion.

The most common *organic* disturbance is a sclerosis of the vessel wall, a condition leading to constant interference with the arterial circulation. Generally a hypertrophy of the left heart follows. If, however, the sclerotic changes are very widely distributed, instead of hypertrophy there may be a dilatation, on account of the resistance being too great for the heart to overcome.

Changes in the *quantity* of the blood, either an increase or a

decrease, are generally only temporary, and soon readjust themselves, either through a contraction or a dilatation of the vessels.

Alterations in the *quality* have a marked effect upon the circulation, probably through the direct action of the toxic substances upon the vessel walls or upon the terminal nerve filaments.

Hyperemia.—*General Hyperemia.*—There may be an increase throughout the body of the total volume of blood. This seldom remains for any length of time, as the various excretory structures of the body get rid of it. The condition known as plethora is the result of persistent overeating and drinking. It is usually associated with a hypertrophy of the left ventricle.

Local hyperemia is an increase in the amount of blood in a part of the body. It may depend upon either an increased supply to the part or be due to a diminished outflow—in one case a dilatation of the arteries, in the other an obstruction of the veins. The first is known as *active* or *arterial*, the second, as *passive* or *venous*, hyperemia.

Active hyperemia is an excess of arterial blood in a part. It occurs with increased functional activity (increased metabolism). It may be brought about through the central nervous system or by direct stimulation of the peripheral nerves. Any pathologic condition that will bring about a local dilatation of the arteries will cause active hyperemia.

The spinal cord or a nerve may be pressed upon as the result of a tumor or of an injury, and a paralytic dilatation occurs. The same condition follows the use of certain drugs acting peripherally either upon the muscular coat of the artery or upon the local nervous mechanism, or both.

In active hyperemia the part affected is redder than normal and more or less swollen as the result of the increased amount of arterial blood that it contains. The temperature is higher than in the surrounding parts, but never higher than that of the internal organs. There is also an increase in the rate of the blood-flow.

This form of hyperemia if continued for some time is followed by (1) hypertrophy of the part on account of the in-

creased nutrition, (2) parenchymatous degeneration from overnutrition or overstimulation of the cells, and (3) a proliferation of the connective tissue around the blood-vessels.

It is found as one of the phenomena of inflammation. Postmortem, it cannot be recognized on account of the contraction of the arterial walls, which drives out the blood. It may persist in the kidneys.

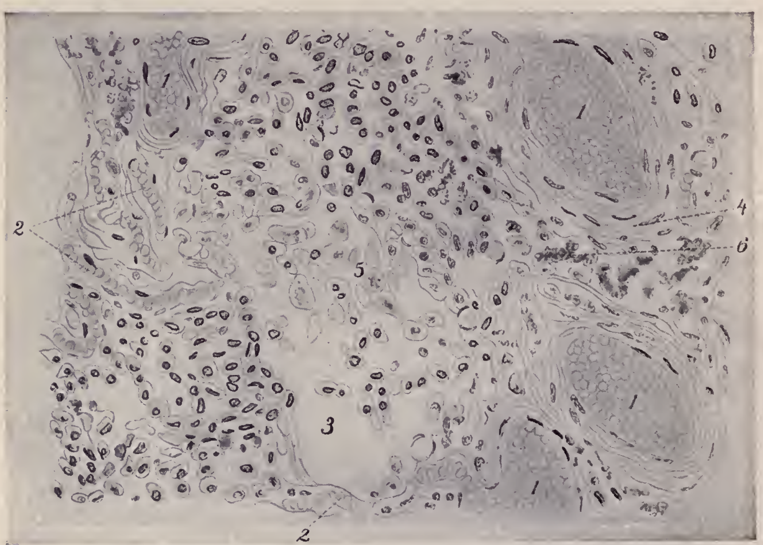


FIG. 1.—PASSIVE HYPEREMIA OF THE LUNG. × 250 (Dürck).
1, Ectatic and distended blood-vessels, filled with blood; 2, engorged and tortuous capillaries; 3, lumen of alveolus; 4, increased interlobular connective tissue; 5, cells, containing blood-pigment, within the alveolar lumen; 6, free, amorphous blood-pigment.

Passive hyperemia is an excess of venous blood in a part. It is the result of a distention of a vein on account of some obstruction to the outflow of the blood. This can be caused by obstruction within the veins or capillaries, as by thickening of their walls, by thrombi, or by pressure from without, as from a tumor. A common cause for general passive hyperemia is a lesion of the heart-valves. The circulation will continue slowly unless the venous pressure becomes as

great as the arterial, when it will stop, a condition known as *stasis*.

A part that is the seat of passive hyperemia becomes cyanotic, swollen, edematous, cooler than normal, and its function less. The rate of blood-flow is lessened. The edema is due to the escape of fluid from the blood. If severe, red corpuscles may escape.

Following long-continued passive hyperemia the tissues will undergo a fatty degeneration on account of the decreased nutrition, or even necrosis and gangrene may result. There may also be some increase in the amount of connective tissue. Pigmentation from escaped hemoglobin is not uncommon—*brown atrophy*.

When *stasis* occurs the blood-corpuscles slowly collect in the smaller vessels, the plasma is exuded, and the cells become packed closely together. Finally, the outline of the cells cannot be seen and the vessels appear to be filled with coagulated blood. Such is not the case, as when the circulation is re-established the corpuscles separate and move along as usual.

Local anemia or *ischemia* is the condition in which the part contains less than its normal amount of blood. It is most commonly due to obstruction by pressure of the flow of arterial blood into a part. This may be due to tight bandaging, pressure from a tumor, or to thrombi or emboli, or to changes in the wall of the vessel.

Disturbances of the vasomotor system may bring about marked lesions. If there is a good collateral circulation the area to which the obstructed vessel goes may show very slight change. If such is not the case, infarction may follow. An anemic area is pale in color, temperature lower, and functional activity decreased.

Hemorrhage is the escape of all the constituents of the blood through the walls of the heart or of the blood-vessels. It is divided into three classes, according to the vessel from which it escapes, as *arterial*, *venous*, or *capillary*.

It may occur by *rhexis*, in which case there is a demonstrable defect of the vessel wall, or by *diapedesis*, when there is

no discoverable lesion. The latter form occurs only from veins and capillaries. The method of escape of the corpuscles is not clear, but is generally supposed to take place through the stigmata of the lining endothelium. Hemorrhage by rhexis may be *primary* or immediate and *secondary* or recurrent; the first following immediately upon laceration of the vessel wall, the second occurring some time after the original injury.

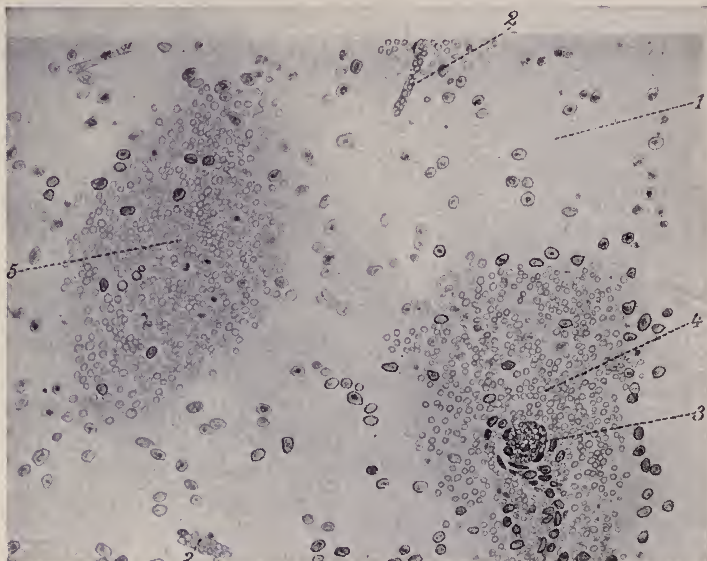


FIG. 2.—MULTIPLE CAPILLARY HEMORRHAGES IN THE CEREBRUM. × 270 (Dürck).

1, Cerebral substance; 2, engorged capillaries; 3, small artery with hemorrhagic infiltration of its walls; 4, hemorrhage by diapedesis in the tissues around a small artery; 5, smaller hemorrhagic foci without any connection with any blood-vessel visible in the section.

Hemorrhages may also be designated by special terms according to the area involved. *Petechiæ* are minute, circumscribed hemorrhages. *Ecchymoses* are of moderate extent; are what are commonly known as bruises. *Extravasations*, *suffusions*, and *sugillations* are conditions in which extensive areas are implicated. A *hematoma* is a collection of blood within a

solid tissue. A *hemorrhagic infarct* is a circumscribed hemorrhage within tissues, the result of the obstruction of an end-artery.

A hemorrhage may also have a special name according to its locality. *Cerebral apoplexy* is a hemorrhage brought about by a rupture of one of the arteries of the brain. According to the cavity in which it collects there may be a *hemothorax*, *hemopericardium*, etc. According to its method of escape from the body it may be known as *epistaxis*, bleeding from the nose; *hemoptysis*, from the lungs; *hematuria*, from the urinary tract, etc.

Hemophilia.—In it no structural changes in the vessel walls can be demonstrated, but severe bleeding takes place as the result of very slight injuries. In such individuals the hemorrhage resulting from the extraction of a tooth may be very dangerous and at times fatal. This condition is generally hereditary and is transmitted by the mother; as a rule the male children manifest the disease, but do not transmit it. On the other hand, the females pass it on to the males, but do not themselves manifest the disease. The most important change, and perhaps the only constant one, to be found in the blood in hemophilia is its lessened coagulability. This may be due to an excessive development of antithrombin, that substance in the blood which prevents coagulation within the vessels under normal conditions. It may be, however, that there is a lack of thrombokinase, the substance which brings about the coagulation of the blood under abnormal conditions. In some bleeders the amount of calcium present in the blood is decreased. Hemorrhage in such individuals has been successfully treated by the injection of normal blood-serum from man or horse. This probably supplies the necessary amount of thrombokinase.

Hemorrhage by rhexis may be caused by: (1) *Increased blood-pressure*, particularly in those cases in which, the blood-vessel walls being diseased, their elasticity is diminished. (2) *Disease of the vessels*, in which the walls become so weak that they are unable to withstand the normal pressure. (3) *Traumatism*, injury of some form sufficient to cause a lesion of the vessel wall.

Hemorrhage by diapedesis may follow in the course of (1) certain *diathetic* diseases, as scurvy, purpura hæmorrhagica, leukemia, hemophilia, etc.; (2) in severe *inflammations;* (3) in severe *hyperemia*, either active or passive; (4) in certain forms of *poisoning*, particularly that by snake-bite; (5) *alterations of innervation;* (6) in *hemophilia.*

Spontaneous arrest of hemorrhage takes place in several ways, but depends upon several factors—the direction of the injury, whether transverse or parallel to the axis of the vessel; the size and nature of the vessel, artery, vein, or capillary; the force of the heart's action and the blood-pressure, and the amount of fibrin-forming substances present in the blood: (1) When a vessel is injured its walls contract and the lumen is diminished in size. The vessel also, being elastic, retracts within the surrounding tissues. (2) The blood, coming in contact with abnormal surroundings, coagulates just outside, then upon, and finally within the vessel; this latter being known as a *thrombus.* In this way the vessel becomes plugged and the bleeding ceases. Another factor is that, as a result of the escape of large amounts of blood, the heart becomes weaker, even to a point where syncope may result; following this the blood-pressure falls and is unable to displace the clot.

The *results* of hemorrhage vary not only according to the amount of blood lost, but also as to the rapidity; if occurring slowly, the blood-forming tissues have time to supply the loss. Then, too, the results depend upon the locality of the hemorrhage, an ounce or so may prove fatal in cerebral apoplexy. If the amount has been small, there will be no ill effects; if comparatively large, weakness and unconsciousness; if very large, death will result from cerebral anemia. When the blood collects within the tissue various changes take place. It undergoes coagulation, a condition in which fibrin factors acted upon by fibrin ferments, in the presence of calcium salts, form a solid body known as fibrin. The greater the amount of fibrin, the more difficult is it for the tissue to recover. The fluid elements are first taken up by absorption by the lymphatics. The corpuscular elements and the fibrin break up, hemoglobin is set free, and the particles are scattered through

the tissue. The greater part will be slowly removed by the phagocytes, but some will remain. If the coagulation has been extensive the tissues may undergo a liquefaction necrosis, giving rise to a cyst.

Thrombosis is the coagulation of the blood within the vessels during life. It may depend upon changes within the blood, changes in the cardiovascular structures, and diminution of the velocity of the blood-flow.

The changes of the blood are those which tend to increase its coagulability. In the formation of a thrombus there is an action of the fibrin ferment or *thrombin* upon certain of the proteins in the blood-plasma. This ferment is not present in the normal circulating blood, but is produced after the blood is discharged from the vessels by the action of *thrombokinase* upon the *thrombogen* of the plasma in the presence of calcium salts. The thrombokinase is supposed to be liberated by the breaking down of leukocytes and blood-platelets. Certain chemical and physical substances—alcohol, ether, chloroform, heterologous blood-serum—when in the circulation may liberate fibrin ferments and thus cause thrombosis. The toxins of pneumonia, of diphtheria, and those resulting from extensive burns are especially active.

The lesions of the vessel walls are particularly important. Fibrin will be deposited upon the wall of the heart or blood-vessels whenever the nutrition of the endothelium of that wall is impaired. Diseases leading to the roughening of the endothelium, particularly arteriosclerosis, are important causes. Inflammation of neighboring structures may bring about changes within the intima. Ligation of a vessel causes an injury to the internal coat, and in that way predisposes to coagulation.

Diminution of the blood-flow may result not only from cardiac disturbances, but also from conditions causing a decrease in the lumen of the vessel. As the current slows, the leukocytes tend to adhere to the wall of the vessel, blood-plates make their appearance, and fibrin is deposited. The nutrition of the endothelium suffers, changes take place in the wall, and another factor in thrombosis then arises. The

appearance of a thrombus depends upon the number of red corpuscles contained within it, and that rests upon the varying rapidity of the blood-current at the time of formation. It is generally made up of superimposed layers of fibrin. After a thrombus has formed there is always a tendency for it to extend up the vessel, against the current of the blood, and to involve successive branches.

If the blood were passing through the vessel with *considerable velocity*, the thrombus would be grayish-white in color, and on section would show well-marked lamination. This is called a *white thrombus*.

If the blood were moving less rapidly, varying numbers of red cells would be entangled in the fibrin and the color would be brown or grayish red, giving rise to a *mixed* thrombus.

If it is formed in a short time from blood that is barely moving, a *red* thrombus will result.

A true thrombus differs from a post-mortem clot within a vessel in that the latter is moister, is never adherent to the vessel wall, and never laminated. The clot may show also a division into pale, "chicken fat," and dark "currant jelly" portions as a result of the coagulation taking place after the heavier red corpuscles have sunk.

Thrombi may be classified according to their *etiology* as:

1. *Infectious*—those depending upon the entrance of bacteria into the circulation.

2. *Mechanical*—foreign bodies free from organisms.

According to their period of *formation* as:

1. *Primary* or *initial* thrombi.

2. *Secondary* or *consequential*, depending upon a pre-existing thrombus and usually extending to the first collateral branch of the blood-vessel.

According to their *morphology* as:

1. *Central*, *occluding*, or *obstructing*—formed by the coagulation of the entire mass of blood contained within a certain portion of the vessel.

2. *Parietal*—when attached to the wall of the vessel, but not completely obstructing it.

3. *Valvular*—parietal thrombi that have become partially detached.

4. *Channeled* or *tunneled*—those in which there still exists a lumen through which the blood can pass. May be the result of secondary changes in old thrombi.

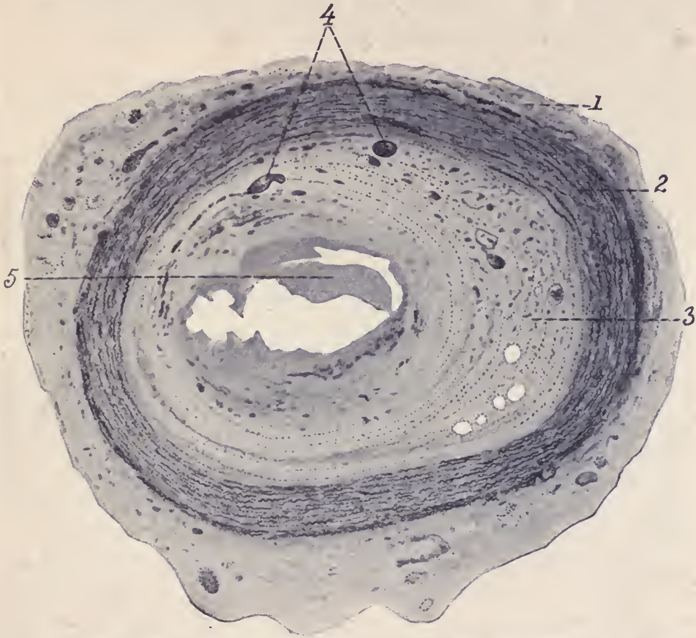


FIG. 3.—ORGANIZED AND PARTLY CANALIZED THROMBUS OF THE BRACHIAL ARTERY. $\times$ 32 (Dürck).

1, Adventitia; 2, tunica media; 3, organized thrombus—*i. e.*, replaced by connective tissue; 4, newly formed and in part dilated vessels within the thrombus; 5, disintegrated remains of the old thrombus.

5. *Ball*—thrombi that lie free within the cavities of the heart, usually in the auricles.

6. *Polypoid*—ball thrombi with pedicles.

Metamorphoses of Thrombi.—The ultimate fate of thrombi depends upon whether they are septic or aseptic. If septic, they must undergo disintegration. If aseptic, they may

undergo *organization*—a condition that is not a transformation into, but is a replacement by, connective tissue.

They may undergo a central *liquefaction* or *softening*. The interior is broken down, blood-pigment set free, and leukocytes in varying numbers are present.

Calcification, particularly of small thrombi, giving rise to either *arterioliths* or *phleboliths*, according to whether they occur in arteries or in veins.

The connective tissue that replaces the thrombi will gradually undergo contraction until only a hard fibrous mass remains, the original lesion becoming converted into a scar.

The new tissue is derived from the endothelium of the blood-vessel and the fixed connective-tissue cells. As it forms, the thrombus undergoes absorption and breaks down into a mass, the granules of which are removed by the leukocytes.

If the thrombi contain living organisms they will be carried through the circulation and give rise to metastatic abscesses in various parts of the body.

The broken-down portions may become lodged in small vessels, and, acting as emboli, give rise to the condition known as embolism.

Embolism is the obstruction, complete or incomplete, of a blood-vessel due to the lodgment of a foreign body within that vessel, the circulating body being known as an *embolus*.

The most common variety of embolus is a dislodged portion of a thrombus, particularly those that occur upon the valves of the heart. Other emboli may be formed by cells of malignant tumors, masses of bacteria, blood parasites, particles of fat, pigment, air, etc.

The most common locality for emboli is within branches of the pulmonary artery, with immediate death or respiratory embarrassment resulting. The condition is most serious when vessels supplying important organs, as the brain, spleen, kidney, etc., are obstructed.

The *varieties* of emboli are: (1) *Simple, mechanical*, or *aseptic;* (2) *specific, infectious*, or *septic*.

The latter is the more severe, as in it suppurative conditions are associated with the mechanical.

Retrograde embolism occurs when, as in whooping-cough, the intrathoracic pressure is increased. An embolus in the inferior vena cava may be carried in a direction opposite to the blood-current and be thus conveyed into the liver through the hepatic vein.

Crossed or *paradoxic* embolism occurs when the foramen ovale remains patulous. In this condition an embolus may

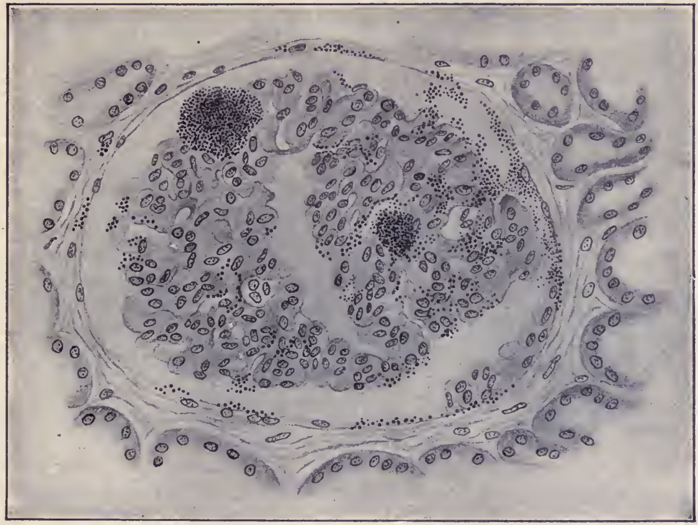


Fig. 4.—Infectious Embolism of the Kidney Following Endocarditis and Showing Groups of Staphylococci in a Glomerulus (Dürck).

pass directly from the venous to the general circulation without going through the pulmonary vessels.

The results of embolism are numerous:

1. *Thrombosis* is a consequence of the stoppage of the flow of blood by the foreign body. The resulting thrombus may be much more extensive than the primary embolus.

2. *Inflammation* of the vessel walls is usually the result of the lodgment of the embolus, particularly if it is of the infectious type.

3. *Atrophy* may follow if the blood-supply is not quite enough for the normal demands, but is yet sufficient to prevent actual death of the tissues.

4. *Necrosis* when the nutrition of a comparatively small area is cut off. Occurs chiefly in the internal organs.

5. *Gangrene* may result if the main artery of a part has been obstructed and the collateral circulation has been insufficient or unable to supply the demands.

6. *Aneurysmal* dilatation, especially in the brain, sometimes results.

7. *Infarction.*

Infarction.—An *infarct* is the area of degeneration and inflammation produced by embolism in an end-artery or where

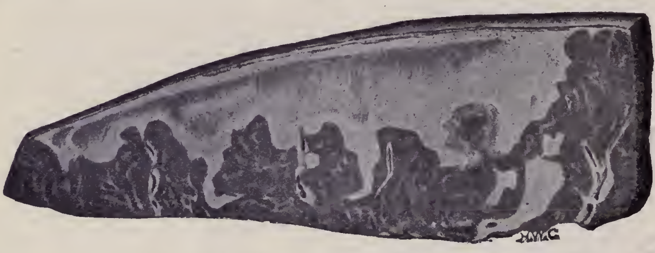


FIG. 5.—PART OF SPLEEN THE SEAT OF MULTIPLE ANEMIC INFARCTS (Coplin).

there is an absence of adequate anastomosis. The act of obstruction constitutes infarction, and must be sufficiently sudden to prevent the establishment of any collateral circulation.

Infarcts occur chiefly in the so-called end-arteries of Cohnheim—those that terminate in veins or capillaries without anastomosis with an artery. They are found particularly in the kidney, spleen, base of the brain and lungs, and sometimes in the heart.

The *varieties* of infarcts are: (1) *Anemic* or *white;* (2) *hemorrhagic* or *red.*

The *anemic* occur more commonly in solid organs, such as the kidney; the *hemorrhagic*, in organs whose structure is loose, as the lungs. The spleen may be the seat of either form.

An *anemic* infarct is one in which there is an absence of

blood. The essential cause of this form is probably the relatively rapid death of the tissues with coagulation before the capillary anastomoses have widened sufficiently to cause hemorrhage. There is usually a narrow hemorrhagic zone surrounding the lesion.

In this type there is probably present a secondary blood-supply sufficient to prevent the occurrence of coagulation necrosis.

A *hemorrhagic* one is where the obstructed area is full of blood. It may be the result of a back flow of blood from the veins (Cohnheim's theory) or from free capillary anastomosis. The latter would be particularly apt to occur when the local or general blood-pressure was previously elevated; or when the lodgment of an embolus caused a reflex contraction of the surrounding vessels and thus brought about an overflow of blood into the occluded area through the capillary anastomoses. Another theory is that the blood does not escape until there has been some degeneration of the vessel walls.

When the blood is cut off a conical shaped area of tissue is deprived of nutrition. As a result, necrosis soon starts in. The apex of this area is directed toward the interior of the organ, the base to the external surface. The base will be swollen and project above the surface of the surrounding tissues.

The infarct is, as a rule, firmer than the rest of the organ, except when it occurs in the central nervous system, where it is usually softer; the firmness depending upon the amount of coagulable material present.

Infarctions of the lung are unusual, as in that organ the capillaries are comparatively large, and the anastomosis between the pulmonary and bronchial arteries may be sufficient to prevent necrosis. To have infarcts occur within the lung, that organ must have been the seat of previous disease.

Results.—Infarction is always accompanied by necrosis and fatty degeneration. (1) The tissue may be restored by absorption and by collateral circulation. (2) It may be replaced by connective tissue with the formation of a scar. (3) It may become encapsulated. (4) Very rarely an infarct may undergo

liquefaction necrosis with cyst formation, particularly in the brain.

Edema, or **dropsy,** is an excess of a clear watery fluid within the tissues between the cells. This fluid differs from the blood-plasma in that it has less albumin, is of a lower specific gravity, is rich in salts, but does not coagulate spontaneously, as it contains very little fibrin. This is called a *transudate* to distinguish it from the fluid present in inflammations, the latter being called an *exudate.*

It may be caused by:

1. Differences of pressure, a filtration process.

2. An increased secretion by the endothelial cells of the vessels.

3. Osmosis, resulting from variations in the relative concentration of salts, particularly sodium chlorid, on either side of the osmotic membranes, the cell walls.

4. The most satisfactory explanation of the occurrence of edema can probably be based upon the properties of colloidal (non-crystalloid) bodies such as gelatin and, presumably, other proteins. If dried gelatin is placed in water it will absorb a definite quantity of that water and will swell up to a certain point. If the water be slightly acidified the amount absorbed becomes very much greater. It has been shown that an inadequate supply of oxygen results in the production in the tissues of acids, particularly lactic acid and carbon dioxid, which, in turn, increase the tendency of colloids to take up water; consequently, edema is brought about. There is probably little of it due to increased capillary pressure or to secretory activity on the part of the endothelium of the blood-vessels.

5. **Neuropathic edema,** as herpes zoster and angioneurotic edema, may be due to something more than simple uncomplicated vasomotor disturbances.

6. **Hydrops,** or **edema ex vacuo,** is that which occurs when an organ, as a result of atrophy, does not completely fill its cavity, the remaining space becoming filled with fluid. It usually occurs in the cranial cavity and in the spinal canal.

The *types of edema* are as follows:

1. **Congestive edema,** the commonest form. Present in

cases of obstruction to the venous outflow. Possibly the interference with the nutrition of the tissues and the changes thus resulting play a part.

2. **Edema from lymphatic obstruction** does not occur in healthy tissues, but does take place if there is some disturbance of nutrition in the areas involved in the lymphatic obstruction.

3. **Inflammatory Edema.**—Probably due to degenerative changes occurring in the endothelial cells of the capillaries and of the tissue cells as well.

4. **Toxic Edema.**—Various toxic substances circulating in the blood have possibly different effects on the capillary walls.

According to the *seat* of the edema, special terms are employed.

When the subcutaneous tissues are generally involved, it is known as *anasarca*. *Ascites* refers to a collection of fluid within the abdominal cavity.

Hydrothorax, a collection within the pleural cavities.

Hydropericardium, when within the pericardium.

Hydrocephalus, fluid within the ventricles of the brain.

Hydrocele, when within the tunica vaginalis testis.

The common clinical causes are: (1) Cardiac insufficiency, the edema usually first noticed about the ankles. (2) Kidney disease, first seen about the eyes. (3) Cirrhosis of the liver, accompanied by ascites. (4) Anemia and cachexia. (5) Pressure upon the veins or lymphatics.

Under the microscope the cells of the involved tissues will appear more or less widely separated and in some instances may be vacuolated.

Interstitial emphysema is an infiltration of the tissues by gas, usually the result of some injury involving the respiratory tract. It may be due to the presence of some gas-producing bacteria, such as the bacillus of malignant edema or the Bacillus aërogenes capsulatus, within various organs, particularly the uterus and liver. It is a comparatively rare condition

CHAPTER V

RETROGRESSIVE PROCESSES

Aplasia signifies a total failure of development of a part. *Hypoplasia* is an incomplete development.

ATROPHY

Atrophy refers to a decrease in the size and in the functional activity of a part. It may be *general* or *local.*

In *general* atrophy the entire body wastes, a condition known as emaciation. It may be the result of lack of food, of starvation, or of disturbances of trophic influences with disorders of metabolism.

In *local* atrophy certain portions undergo changes which may be either *simple, degenerative,* or *numerical,* as the latter is sometimes called.

In the simple variety the individual cells undergo a decrease in size.

In the degenerative the number of cells is reduced as a result of disease. This is not considered a condition of true atrophy.

Atrophy may be brought about by there being no longer a demand made upon the part. Through lack of use the cells become smaller.

Old age is often accompanied by atrophy; is seen particularly in the sexual organs and in the loss of the elastic tissue of the skin.

Pressure is one of the commonest causes; occurs as a result of tight lacing, etc.

Interference with the blood-supply on account of the part not being supplied with a proper amount of nutrition.

Disturbances of the trophic functions, as in poliomyelitis.

The atrophied part will be smaller than normal, and fre-

quently very irregular, causing elevations and depressions. Microscopically, the cells will be reduced in size, more or less degenerated, and frequently pigmented. The latter condition occurs commonly in the heart and is known as *brown atrophy.*

DEGENERATIONS

Degenerations of cells can be divided into two forms:

1. *Infiltrations*, in which abnormal substances are deposited within the cells.

2. *Metamorphoses*, in which the protoplasm of the cell is transformed into abnormal substances.

"It was thought, but now seems less certain, that we could distinguish two processes which might accompany each other: one, the change wrought in the cytoplasm itself, leading to the appearance in the cell of such changed products; the other characterized by the appearance in the cytoplasm of substances obtained from outside the cell, and, it may be, imperfectly handled by the cell. It was thought that the former were degenerations proper and the latter infiltrations, but further study shows that it is becoming increasingly difficult to separate the two; that, in fact, they are too closely related to permit of being considered apart. Especially does it seem to be that true infiltration by itself is a rare occurrence. 'Infiltrated' materials, as fat, glycogen, etc., probably are the result of synthetic processes."

The changes in the cell may also be either *quantitative*, as when a normal substance is present in an abnormal amount; or *qualitative*, when there is an abnormal substance present.

Necrobiosis refers to the molecular or cellular death of a part.

Parenchymatous Degeneration or Cloudy Swelling (Fig. 164).—In it the protoplasm of the cells contains an increased amount of protein substances. It accompanies very slight disturbances of nutrition, such as occur in inflammation, is found in all infectious diseases and intoxications, possibly as a result of increased bodily temperature, most likely as a result of disturbances of metabolism.

Although all the cells of the body, both glandular and stroma, may undergo this change, they are not equally affected, the

glandular ones being more liable to injury. The secreting cells have as their function the removal of certain substances from the body. If the blood contains injurious materials, these cells naturally will be the first affected, as they are the more intimately concerned.

This degeneration may follow extensive superficial burns, probably as a result of the action of the poisonous substances absorbed.

Microscopically the individual cells will be swollen and larger, more granular, and more opaque than normal on account of the presence of minute granules; the nucleus, consequently, may be obscured. These latter are insoluble in alcohol and ether, but are dissolved by alkalies and weak acetic acid.

The function of the cell is more or less disturbed, but complete recovery frequently occurs. If, however, the cause persists, fatty metamorphosis results.

Fatty infiltration is the deposit of fat within the cell or intercellular tissues. In all parts of the body, except the liver, the connective tissue is affected. In this organ the secreting or parenchymatous cells are involved. May be *general* or *local*. It may occur in cells that normally contain no fat, or else appear in excess in cells that do contain it.

The fat contained within the cells is made up of neutral palmitin, olein, and stearin.

Fatty infiltration may be *hereditary*, as obesity in successive generations; may result from *excessive nutrition*, particularly if combined with *lack of exercise*.

The use of *alcohol*, especially in the form of malt liquors. The alcohol, being easily oxidized, probably takes the place of the fats which remain unused.

Anemia, on account of the insufficient oxygenation of the tissues.

In certain *cachectic* conditions, as in phthisis; where the liver is frequently filled with fat.

The most common seats are the subcutaneous and subserous tissues, the omentum and the mesentery, in the liver, heart, kidney, and between the muscle-fibers.

Certain other regions, such as the subcutaneous tissue of the penis, nose, ear, lips, and eyelids, are never involved.

An organ the seat of fatty infiltration is larger, paler, mottled, streaked or diffusely yellow, softer, more friable, and greasy on section.

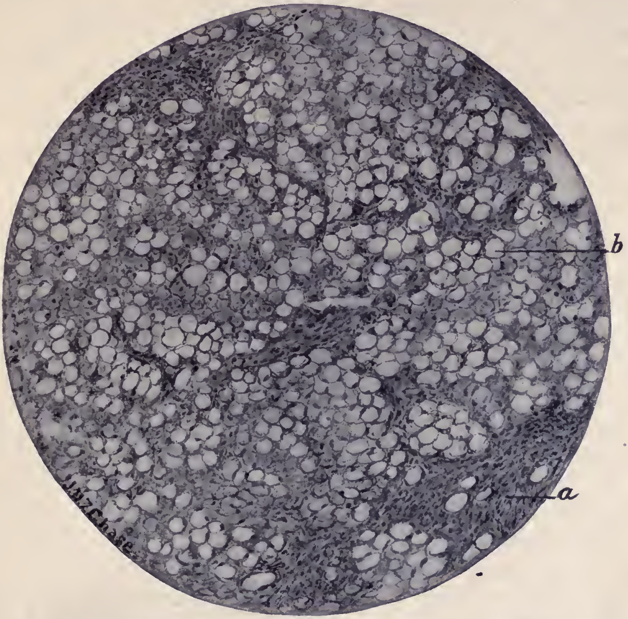


FIG. 6.—FATTY INFILTRATION OF THE LIVER (McFarland). *a*, Periportal connective tissue; *b*, fat drops in liver cells.

Under the microscope the fat may be found either inside or outside of the cells. If outside, it is most marked along the fibrous bands.

Inside the cell, particularly the glandular variety, the fat occurs in droplets which tend to enlarge and coalesce. The nucleus is displaced, giving the "signet-ring" appearance, or obscured; is seldom destroyed. The cell wall remains intact.

The *tests* for fat are sudan III, which stains it scarlet, or a 1 per cent. solution of osmic acid, which stains black. It

is soluble in alcohol, ether, and xylol; insoluble in water, acids, and alkalies.

Adipocere refers to the transformation of the fats into a wax-like substance most common in bodies that have been buried in damp earth.

Fatty metamorphosis is a conversion of the cell protoplasm into fat.

Generally speaking, the causes of cloudy swelling will bring about fatty degeneration if they are severe enough or act for a sufficiently long time. It occurs in *senility*, particularly when associated with marked arteriosclerosis and atheroma; in *anemia*, either as a result of hemorrhage or in diseases such as leukemia and pernicious anemia. The condition is probably more widespread in the latter than in any other disease. Occurs also in long-continued and high fever.

The most important substances causing the metamorphosis are the *poisons*, as the metallic salts, chloroform, coal-tar products, etc., and those formed by micro-organismal activity, as in yellow fever.

The fat present in the cells is either (1) formed by actual disintegration of the protoplasm of the cells, or (2) is taken up by the cells from the blood and remains unaltered, owing to defects in the vital power of the cell to assimilate it.

This condition may result from—

1. Insufficiency of the supply of nutriment.

(*a*) The blood-supply may be actually diminished.

(*b*) There may be increased work without a corresponding increase in the blood-supply.

(*c*) Actual deficiencies in the blood may impair its nutritive value, as diminution in the hemoglobin or of the corpuscles.

2. The failure of the cell to make use of the material placed at its disposal is probably the more important cause.

(*a*) The result of bacterial toxins.

(*b*) The influence of inorganic poisons.

(*c*) A senile change dependent upon the exhaustion of the inherited vital capacities of the cells.

Organs undergoing this change are generally smaller and

paler, yellowish, soft and flabby, and easily friable; they may undergo caseation.

The liver in yellow fever is a typical example.

Microscopically the cell protoplasm contains a large number of minute droplets that rarely coalesce. The nucleus is soon involved and ultimately is destroyed. The entire cell may break down into a fatty granular mass, sometimes called a "compound granule cell." Granules may be so small that their character cannot be recognized except by special staining.

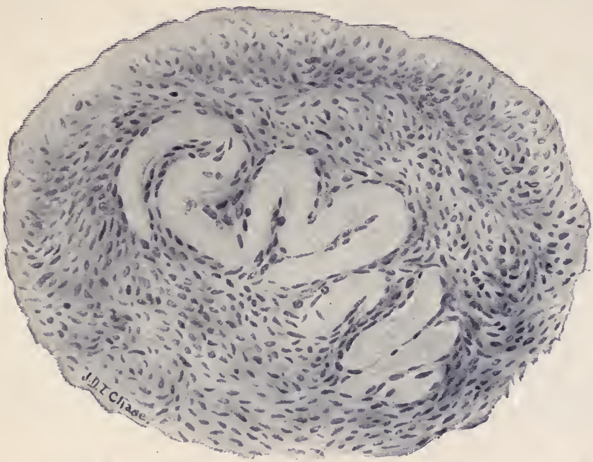


FIG. 7.—HYALINE DEGENERATION OF AN OVARIAN CAPILLARY. Oc. 2; ob. 9 (McFarland).

To distinguish between fatty metamorphosis and fatty infiltration is frequently not only difficult, but impossible, especially so in the liver. The droplets may coalesce in metamorphosis and remain separate in infiltration.

Crystals of margarin and the notched rhombic plates of cholesterin are frequently found in the fatty areas.

Hyaline metamorphosis is a conversion of cells and intercellular substance into hyaline material.

The cells of the connective tissue are most frequently involved, but epithelial and muscle cells may be affected.

The hyaline material occurs in the form of granules, is glistening and waxy, and with Van Gieson's method stains intensely red. Has no specific action with iodin.

It is at times scarcely distinguishable from amyloid metamorphosis.

It is found as a result of infectious diseases, septic processes, in chronic intoxications, such as lead-poisoning, and in new

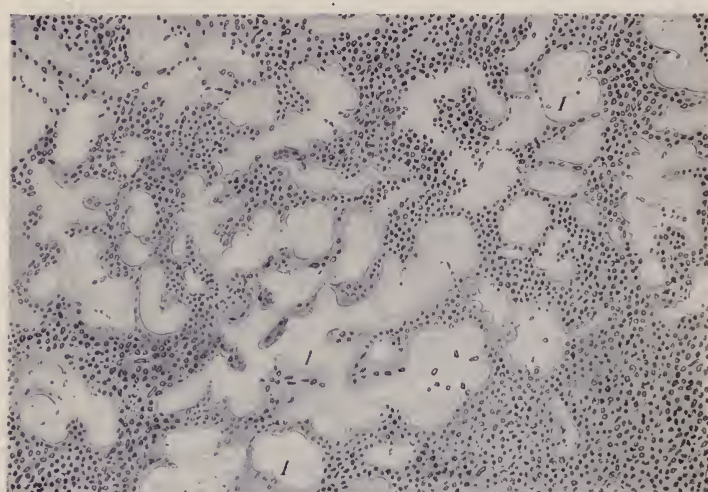


FIG. 8.—HYALINE DEGENERATION OF THE RETICULUM OF A LYMPH-GLAND IN TUBERCULOSIS. × 280 (Dürck).

Among the lymphocytes are seen single reticular fibers, which are greatly thickened and transformed into shining, homogeneous, non-nucleated bars (1).

growths. Its formation is probably dependent upon some malnutrition of the tissues. Generally this form of degeneration is not sufficiently extensive to be recognized by the naked eye.

The most common site is in the endothelial and subendothelial tissues of the blood-vessels. The lumen will be narrowed or obliterated according to the extent of the thickening of the wall.

It also frequently occurs in the interstitial tissues, as between the renal tubules, between muscle-fibers, hepatic cells,

and in the reticulum of lymph-nodes (Recklinghausen's degeneration). A third site is within the cells, particularly those of mesodermic origin.

It is either formed within the cell or, being formed elsewhere, has been brought to and deposited within the cell.

Mucoid or **myxomatous metamorphosis** is the conversion of cells and intercellular substances into mucin.

Mucin is insoluble in water, but will absorb it; is soluble in alkaline solutions, but is precipitated by weak acetic acid. When boiled with acids, will reduce Fehling's solution.

Either epithelial cells or the intercellular substances may undergo mucoid change. The latter is the more truly a metamorphosis.

It occurs in epithelial cells in all forms of catarrhal inflammation, in the cells of epithelial cysts, and in some carcinomata.

It is found in the interstitial tissues in both epithelial and connective-tissue growths, in some inflammatory conditions, and in myxedema.

The mucous membranes will be covered by a coat of thick, stringy, and viscid exudate. The underlying tissues may or may not show congestion.

Connective tissues will be more or less soft, slightly swollen, and will tear easily. If the condition is very much localized, cysts filled with mucin may be found. Three substances closely related are included under the heading of Myxomatous metamorphosis: *mucin*, *pseudomucin*, and *paramucin*, each one differing slightly from the others in its reaction.

The typical mucoid cell is the so-called "goblet-cell" that is found in the large intestine.

The mucoid change looks under the microscope very much like edema. The cells are widely separated and the structure of the tissue is poorly defined. The cells frequently stain poorly and degenerate.

Colloid metamorphosis is the transformation of the cell substance into a thick, sticky substance known as colloid. It is found only in epithelial cells. It is not precipitated by acetic acid or by alcohol, nor does it swell in water. It usually stains orange color with Van Gieson.

It is normally found in the acini of the thyroid gland and in the pituitary body. It is frequently found in parovarian cysts, in goiter, in the tubules of the kidney in chronic nephritis, and in the prostate gland.

In cysts the colloid material is generally contained in many small cavities, giving rise to a honeycomb appearance. It may be transparent, yellowish, bluish, or chocolate color, according to other substances present.

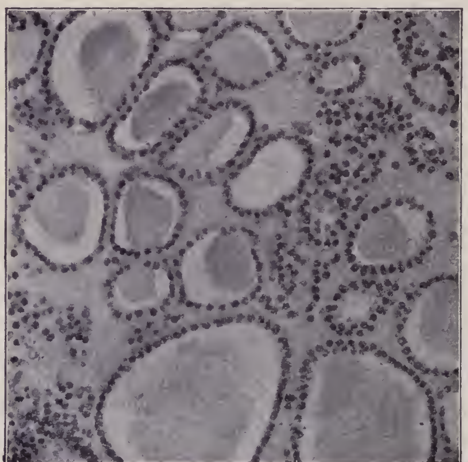


Fig. 9.—Colloid Degeneration of the Thyroid Gland, Showing Masses of Colloid Matter in the Gland Acini (Karg and Schmorl).

Amyloid metamorphosis is a degeneration of the connective tissues into an abnormal substance giving an amyloid reaction. The origin of this material is obscure. It may be formed *in loco*, but more probably is brought to the tissue from some other part of the body. It does not exist as much in the blood, but is very probably derived from substances contained in that fluid. Some believe that the leukocytes, others that the erythrocytes, are the cells from which it is derived.

It is frequently called *waxy*, *lardaceous*, or "*bacony*" disease; is found in the intercellular portions of the connective tissues and not in secreting cells.

It is found as a result of long-continued suppuration and ulceration, such as occur in diseases of the bone, chronic tuberculosis, syphilis, leukemia, and dysentery.

The organs most commonly affected are the spleen, liver and kidney, the larger blood-vessels, the mucous membrane of the intestines, the lymph-nodes, and the heart.

The involved organs are generally pale, larger, firmer, and heavier than normal, and with rounded edges. The cut surface is smooth, glistening, and transparent, either diffuse or

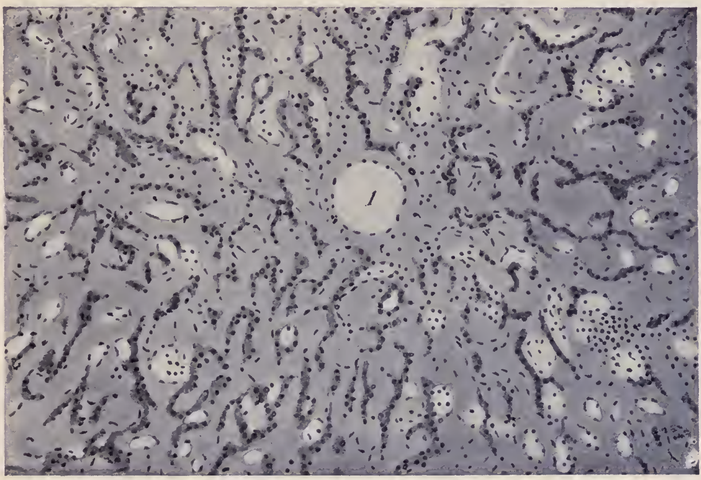


Fig. 10.—Amyloid Degeneration of the Liver. × 98 (Dürck).
1, Central vein. Portal capillaries surrounded by homogeneous masses and bands; the epithelial lining distinct. Columns of liver cells compressed to narrow, atrophic strips.

localized. The usual sites of the degeneration are the walls of the capillaries, in the intima and media, the adventitia being rarely affected.

In the kidney the capillaries of the glomeruli are first attacked, converting the bodies into waxy, homogeneous masses; finally the connective tissue may be involved.

In the liver the amyloid substance is found between the peri-

5

portal connective tissue and the central vein, in the intermediate zone which is supplied by arterioles and capillaries of the hepatic artery. In the spleen it may give rise to the "sago spleen," a condition which is brought about by the formation of amyloid material in the Malpighian bodies. Later on, the organ may become very extensively involved. In some cases the vessels in the trabeculæ of the organ may be the seat of the metamorphosis.

When amyloid material has been once deposited it is practically never removed. It is insoluble in water, alcohol, ether, dilute acids, alkalis, etc. Resists peptic digestion and withstands decomposition for a long time. Unless special staining methods are employed, it frequently cannot be distinguished from hyaline degeneration.

When the affected tissue is placed in Lugol's solution (iodin 1, potassium iodid 2, water 100) the amyloid substance becomes a mahogany brown. If stained in 5 per cent. aqueous gentian-violet the amyloid will appear pink; the normal tissues, blue.

If after staining in iodin, weak sulphuric acid (5 to 10 per cent.) is added, the amyloid will turn blue.

Corpora amylacea, or amyloid bodies, are found in the prostate gland, in lymphatic nodes, and in the central nervous system. They are concentrically striated like a starch granule, and although in their reaction they may resemble starch and amyloid, they are probably neither.

Glycogenic infiltration is a deposit of glycogen within the cells. It is found normally in small amount throughout the body except in the mammary glands and central nervous system.

It is greatest in amount in the cells of the liver, in voluntary muscles, and in the kidneys; is also present normally in the blood, both in the plasma and in the cells, particularly the polymorphonuclear leukocytes. It is also commonly found in malignant tumors of mesodermic origin (sarcomata).

The origin of the glycogen is not clear; it is a carbohydrate, but seems to be derived from protein and carbohydrate substances. Glycogen is most frequently found in the condition known as diabetes.

Tissues containing large amounts of glycogen may have a distinct hyaline appearance. The reactions, however, differ, as it is soluble in water, but not in alcohol, ether, or xylol; is colored a brownish red on the addition of tincture of iodin 1 part, absolute alcohol 4 parts. The brown is not changed to blue on the addition of sulphuric acid.

Microscopically, glycogen occurs in the cells in clear, colorless droplets, usually near the nuclei.

Serous or **edematous infiltration** is a condition of dropsy of the cells. All kinds of cells may be involved, but it is most common in the epithelial. It is an absorption of an excess of plasma by the cells.

It may accompany general dropsy or result from inflammation; is also found in tumors.

The part involved is usually enlarged, spongy, and edematous.

The cells are distended and filled with large and small vacuoles in the protoplasm and at times within the nucleus.

Pigmentary infiltration is the deposit of pigment within the tissues.

According to their origin, pigments may be divided into four classes:

1. Those derived from outside of the body.

2. Those formed from hemoglobin and its derivatives, the hematogenous pigments.

3. The hepatogenous or biliary pigments.

4. Metabolic pigment; that resulting from cellular activity within the body is known as melanin.

The *hematogenous* pigments are three—*hemoglobin*, *hemosiderin*, and *hematoidin*.

Hemoglobin is dark red in color, amorphous, contains iron, and is soluble in alcohol, ether, and chloroform. It is recognized chemically by the addition to the suspected fluid of a few drops of a fresh tincture of guaiac and then followed by an ethereal solution of hydrogen dioxid. The mixture, which is at first milky white, turns a deep blue.

If the dried blood is dissolved in normal salt solution, then warmed and evaporated, glacial acetic acid added and warmed, small reddish-brown rhombic plates of hemin appear.

When brought in contact with sulphuretted hydrogen, hemoglobin combines and forms ferrous sulphid, which is black. This gives rise to the bluish discoloration of the abdominal wall that appears when decomposition has occurred.

Hemoglobin is set free from the erythrocytes through hemolysis, either within the vessels or when the blood has escaped into the tissues. The surrounding structures will be diffusely stained. This is commonly seen post-mortem, particularly in those parts of the liver that are in contact with the intestines. When it is set free within the vessels during life, it may be deposited within the lymph-nodes, spleen, and kidney, forming pigment metastases.

Hemosiderin is yellowish or brownish in color, amorphous, contains iron, and is insoluble in water, alkalis, alcohol, ether, xylol, and chloroform.

On the addition of potassium ferrocyanid and weak hydrochloric acid it turns blue (Prussian blue reaction).

It occurs in the blood, in cells and intercellular tissues, as a consequence of recent hemorrhages; apparently results from the slow destruction of the erythrocytes.

The granules are taken up by the phagocytes and may be finally removed by them. Cells filled with the granules are frequently found in the sputum in cases of chronic congestion of the lungs.

Hematoidin, similar to bilirubin, is a reddish-brown pigment, found in the form of rhombic crystals; does not contain iron, is insoluble in water, alcohol, or ether, but is soluble in chloroform. It is found at the seat of old hemorrhages, and is generally considered a later form of hemosiderin.

The *causes* of hematogenous pigmentation can be divided into local and general.

Local.—Hyperemia, venous stasis, inflammation, hemorrhage.

General.—Hemolysis resulting from animal poisons, bacterial toxins, chemicals. Action of parasites, as in the destruction of the red cells in malaria.

Hepatogenous pigmentation is due to the presence of pigments derived from the bile, *bilirubin*, which is similar to

hematoidin, and its oxidation product, *biliverdin*. The bilirubin is formed by the hepatic cells from hemoglobin, from destroyed red blood-cells, the iron being retained in the liver and not cast off along with the pigment. It is soluble and consequently is taken up by the blood and carried throughout the body, giving rise to the discoloration known as *icterus* or *jaundice*. Both cells and intercellular substances may be diffusely stained, or, if the condition is of long standing, greenish-yellow crystals or granules may be found.

Fig. 11.—Brown Atrophy of the Heart-muscle in Longitudinal Section (Dürck).

The fluids of the body will also be discolored.

The presence of these pigments can be recognized by *Gmelin's* test with fuming nitric acid, which will give a play of colors at the point of contact.

This condition may be caused by (1) obstruction to the outflow of bile through the ducts, *obstructive jaundice;* (2) possibly through excessive bile formation resulting from hemolysis, *hematogenous jaundice;* (3) hepatic disorders, as acute yellow atrophy of the liver.

Metabolic pigmentation or *melanosis* is a discoloration of the tissues through the formation of *melanin* by the cells.

The tissues are colored yellow, brown, or black.

Under the microscope melanin occurs as dark granules in the

cells and intercellular tissues. Is normal in the pigmented cells of the retina, choroid, hair, and skin.

Its chemistry is not well known. It contains sulphur, but little or no iron, is insoluble in water, alcohol, and ether, but soluble in boiling alcohol, acids, and alkalis.

It is found commonly in the *melanotic sarcoma*. It generally tends to destroy the cells in which it is contained, and for

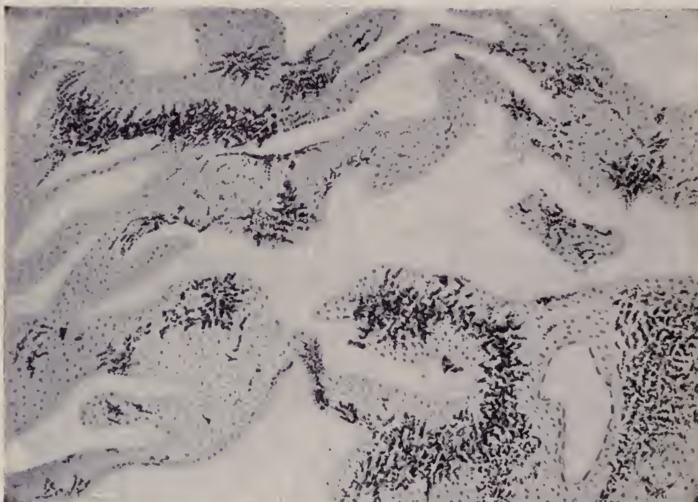


FIG. 12.—ANTHRACOSIS OF THE LUNG. × 100 (Dürck).

The lung tissue is very much indurated as the result of newly formed connective tissue in which are embedded star-shaped masses of fine, granular, blackish pigment of inhaled coal particles.

some reason such tumors are generally more rapidly metastatic and fatal than the non-pigmented forms.

In *Addison's disease* there is a general bronzing or melanosis of the skin. In many cases this condition seems to follow extensive disease of the adrenals.

In *malaria* the pigment present is probably not melanin, but is similar to hematin, and is formed by the action of the malarial parasite upon hemoglobin.

Certain *muscular degenerations*, as in "brown atrophy"

of the heart. Is questionable whether such granules are true melanin. Various *skin affections*, as freckles, or *lentigo*, *chloasma*, and also in *pigmented moles*.

Extraneous pigmentation results from the introduction of coloring-matters into the body from the outside. The tissues most commonly affected are those of the lungs, giving rise to the condition known as *pneumonokoniosis*.

Anthracosis, or the deposition of coal-dust, is the most frequent, the lungs being colored more or less black according to the amount present.

Siderosis results from the inhalation of fine particles of iron.

Chalicosis, caused by the presence of lime in the lungs.

Argyria is a bluish-gray discoloration of the skin resulting from the long-continued use, internally, of nitrate of silver.

Tattoo marks following the introduction of insoluble coloring substances into the skin.

Calcareous infiltration or **calcification** refers to the deposit of earthy salts within the tissues. It occurs in consequence of a deficiency of oxygen and an excess of carbon dioxid in the tissue juices, which causes a deposit of the carbonates and phosphates of magnesium and calcium. Oxalates are also generally present.

This process is found only in those tissues that are either completely destroyed or else undergoing degeneration as a result of imperfect nutrition.

The deposition of the salts is probably due to a lack of oxygen and an increase of carbon dioxid in the tissues, on account of which there is a precipitation of the magnesium and calcium carbonates and phosphates.

It is commonly seen in the fibrous framework, but may be found within the cells as well. The favorite site is in the connective tissues that have a poor blood-supply, such as cartilages, the walls of blood-vessels, also in old inflammatory areas, in regions of degeneration, such as infarcts, around foreign bodies, and in tumors, particularly in degenerated uterine fibroids. Is sometimes seen in the ganglionic nerve-cells, in the "pearls" of epitheliomata, and in the tumors of the nervous system called *psammoma*, which are made up of masses

of salts deposited in the tissues. The most common seat is probably in the arterial system. It is often the sequel of a senile atrophy of the elastic tissue of the vessel wall, along with degeneration of the connective tissue and a general fibrosis.

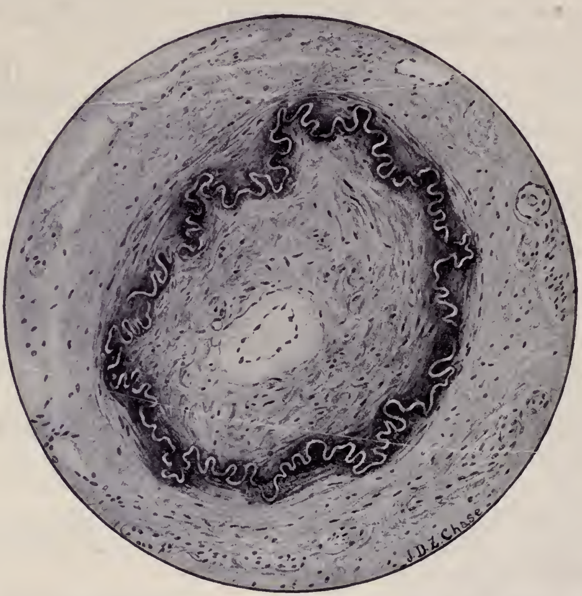


FIG. 13.—CALCAREOUS INFILTRATION OF THE WALL OF A SMALL ARTERY FROM THE WALL OF A GUMMA OF THE LIVER. Zeiss, Oc. 2; ob. D. D. (McFarland).

In addition to the calcification that has occurred in the media contiguous to the fenestrated elastic layer, there is marked syphilitic endarteritis with great reduction in the caliber of the vessel from proliferation of the subendothelial tissue of the intima.

The valves of the heart frequently undergo calcification, as well as the walls of the aorta, the coronary, and cerebral arteries.

Microscopically the salts may appear as granules, spicules, plates, or crystals.

If within the cellular protoplasm the granules may be so numerous as to hide the nucleus.

The salts are insoluble in ether, but give off carbonic acid gas when dissolved by hydrochloric acid. They also stain very deeply within hematoxylin.

Uratic infiltration in the form of sodium biurate occurs in the cartilages and fibrous tissues in gout. Ordinarily the above salt is soluble in the blood, but under certain constitutional conditions it is deposited as an insoluble salt. These collections are called *tophi*, and are found particularly in the joints. An admixture of calcium and magnesium carbonate and phosphate is usually present.

Necrosis is the death of a part of a living organism. It is the death of a part as distinguished from the death of the entire body (somatic death). The causes of necrosis are (1) *local injury*, (2) *vascular obstruction*, and (3) *trophic disturbances*.

Under the local injuries are included those that are mechanical, chemical, thermal, and bacterial.

Mechanical injuries may cause destruction of the cells directly or by interference with the blood-supply. Pressure of foreign bodies will often bring about necrosis.

Chemical substances such as the acids and alkalis may cause destruction of the tissues.

Thermal injuries, those from extreme heat or cold, will more or less quickly destroy the vitality of the cells.

Bacterial products acting as toxic agents will frequently cause necrosis and gangrene.

If vascular obstruction take place suddenly, the nutrition will be shut off and necrosis result.

Trophic disturbances will lessen the resisting power of the tissues with subsequent necrosis. This is seen in decubitus or bed-sore that occurs in various forms of spinal disease. The perforating ulcer of the foot is another example.

The cells in the necrosed areas will show different stages of disintegration. The cell wall may remain, but the cytoplasm will not stain. There may be complete destruction and breaking down of the cell. The granules in the protoplasm disappear, and it in turn becomes cloudy, gradually breaks up, and vacuoles form. The nucleus may lose its staining power or may undergo destruction in one of two

ways: By *karyorrhexis*, a breaking down of the chromatin into granules, or by *karyolysis*, a liquefaction of the nuclear constituents.

Necrosis may be of different varieties.

Coagulation necrosis is a form of death of those tissues freely supplied with lymph, accompanied by a consolidation of the protein contents. It is a change similar to the coagulation of the blood. The fibrin ferment present acts upon the fibrin factors and fibrin is formed.

It is found in thrombi, blood-clots, and interstitial hemorrhages.

Occurs in various inflammatory exudates, particularly in croupous pneumonia and diphtheria, and in infarcts.

The seat of the necrosis is firmer and paler than normal, and dry. Later on it may become softer and discolored as a result of disintegration of blood.

Caseous necrosis is a condition in which the tissues have been transformed into a cheese-like substance.

It is found only as a sequel to pre-existing coagulation necrosis. Is found most commonly in tuberculosis, but occurs in tumors and in syphilis.

Surrounding the area of caseation there is generally a zone of coagulation.

Liquefaction or *colliquation necrosis* is the death of the tissues with liquefaction. It occurs in those tissues that contain little protein substance, especially in anemic infarcts of the brain. The nervous tissue undergoes a softening, becomes semi-fluid, and eventually liquid, remaining as a colliquation cyst.

Focal necrosis is a condition in which minute areas of necrosis scarcely visible to the naked eye occur, particularly in the lymph-follicles and the liver in various forms of severe infection. They may be due to minute thrombi or to alterations in the endothelium of the capillaries.

Gangrene may be of two forms—dry and moist. The tissues involved are those that are exposed either directly or indirectly to the atmosphere.

Dry gangrene, or *mummification*, is the death of tissues with

subsequent drying. It occurs particularly in the extremities of old people or of those who are much debilitated. Is generally due to some obstruction of slow formation of the arterial system, by a thrombus, an embolus, by disease of the walls, by a spasmodic contraction of the vessel, or by pressure from the outside. It is usually circumscribed, there is very little odor, the tissues become almost black and mummify through evaporation of the moisture.

Moist gangrene is the death of living tissues plus an infection by bacteria that are capable of producing putrefaction.

It occurs in those parts that are exposed to the air, either directly or indirectly.

It takes place in people who have previously been in good physical condition, usually being the result of extensive venous obstruction combined with a weak arterial supply.

The part involved undergoes necrosis and afterward becomes infected. It becomes greenish black, gas blebs appear on the skin or in the tissues, and an extremely offensive odor develops.

The cells break down completely, hemorrhage takes place as a result of destruction of the blood-vessels, and many toxic substances are formed. They resemble the alkaloids and may bring about marked disturbances of the organism. This form of gangrene may terminate in several ways.

The dead tissue, *sphacelus* or *slough*, gives rise to a zone of inflammation, which is known as the *line of demarcation*, at the point of contact with the healthy tissue. This zone, as a rule, indicates the limits of the gangrenous process. At this site there is a constantly increasing interval between the dead and living tissue. The tissues here break down and form the *line of ulceration*. It is an attempt of nature to throw off the foreign substance and at the same time to form new tissue. The process is known as *exfoliation*. If the necrotic tissue cannot be thrown off, as is the case when bone is involved, there will probably be a *sequestrum* formed. This is the result of new bone forming around the dead tissue before there has been time for it to exfoliate.

If the degenerated area cannot be discharged, as when the

internal organs are involved, it frequently becomes surrounded by a capsule of connective tissue that protects the neighboring parts—process of *encapsulation.* Again, the necrotic tissue

FIG. 14.—SENILE DRY GANGRENE OF THE LOWER EXTREMITY, SHOWING LINE OF DEMARCATION (Hektoen).

may disappear through *absorption*, may *calcify*, or undergo *cicatrization* or *organization.*

Fat necrosis is a peculiar type occurring usually in the fat

within the abdominal cavity. In nearly all cases it seems to be dependent upon some disease of the pancreas, particularly hemorrhagic pancreatitis.

It is the result of the splitting of the fat molecule into its fatty acid and into glycerin. The fatty acids are deposited as crystals and unite with calcium to form salts.

These areas are generally about the size of a pea, whitish in color, soft or gritty. A zone of inflammation may or may not surround them.

Death is the cessation of life—meaning that all the component parts of the organism cease to live.

Up to a certain time the cells of the body are able to supply all the needs, but eventually the natural term of life is reached and the cells gradually fail to support the tissues. Such a condition would be termed *physiologic* death. If, however, it follows as a result of diseased processes, it would be *pathologic*.

The two, however, cannot be strictly separated, as in old age there are always conditions present that are not normal.

The conditions absolutely necessary for life are a continuation of *circulation*, *respiration*, and *innervation*.

There may be a destruction of certain portions of the body without death following, but a cessation of any of the above-mentioned functions brings about dissolution. This is known as *somatic* death, and, according to which function ceased, it is said to have taken place by *syncope*, *asphyxia*, or *coma*.

Molecular death refers to the death of cells.

Signs of death are those that indicate that the organism has ceased to live. Cessation of the necessary functions may give rise to *apparent* death, but without other indications it cannot be diagnosed with certainty.

The necessary signs are:

Algor mortis, a fall of the temperature to that of the surrounding atmosphere. Following tetanus it may, however, be preceded by a distinct rise, continuing for some hours.

Livores mortis, or *post-mortem lividity*, are the discolored areas that appear in the dependent portions of the body as a result of the dilatation of the blood-vessels. It is often of great im-

portance to distinguish this condition from the discoloration following a blow. In the first the color will disappear on pressure, but in a bruise it will remain, as the blood is not within the vessels.

Rigor mortis, or *post-mortem rigidity*, is a stiffness due to the coagulation of the albumin of the muscles with the formation of myosin. It is first seen in the muscles of the neck and jaws, then extends downward, involving the entire body.

It generally comes on within four to twelve hours, but may appear immediately or be delayed for twenty-four hours. At the end of twenty-four to forty-eight hours it usually passes off.

If death has occurred suddenly and the individual is in good health, it appears much more quickly than when death has taken place slowly.

Decomposition is the infallible sign. Its appearance depends upon the surrounding temperature, taking place more quickly in hot weather. It is first noticed as a greenish discoloration of the abdominal wall, and is due to the sulphuretted hydrogen from the intestines acting upon the iron contained within the hemoglobin.

The tissues soften and there is more or less odor, due to the formation of various gases.

Loss of elasticity, *relaxation of the sphincter muscles* and *loss of transparency of the cornea*, and *dilatation of the pupils* complete the list.

Apparent death may occur in hysteria, catalepsy, submersion, cholera, exposure to cold, and action of electricity. It is detected by the absence of the signs of true death. The tissues will appear reddish if a light is held behind them, blood will flow from a wound, moisture will collect on a mirror held in front of the face, and the muscles will react to electricity.

CHAPTER VI

CELL DIVISION

As a result of the tissue injury in disease, repair is brought about by cell multiplication or reproduction. The extent of this regeneration depends upon the degree of specialization of the tissue.

The Cell.—The adult cell consists primarily of a mass of *protoplasm* or *cytoplasm* surrounded by a limiting membrane called the *cell wall*, and containing a *nucleus* within which there may be a small body called the *nucleolus*.

The *cytoplasm*, which is a semifluid substance, is divided into two portions—the *spongioplasm*, which consists of a very elastic and extensible framework, and the *hyaloplasm*, which is homogeneous and less active.

Embedded in the cytoplasm are minute granules known as *microsomes*. These are most numerous toward the center of the cell; the peripheral zone, called *exoplasm*, not containing them.

Foreign bodies and vacuolations may also be found within the cell.

The arrangement of the constituents of the cytoplasm varies at different times. Frequently the spongioplasm is arranged as a distinct reticulum. This is, however, not permanent, and seems to depend upon the relative proportion of the hyaloplasm.

The *nucleus* is confined by a distinct wall, the *nuclear membrane*, within which is the nuclear substance or *karyomitome*. This is divided into a framework of fibrils, the *nuclear fibril*, and an interfibrillar substance, the *nuclear matrix*.

The fibrils consist of a part called *chromatin* or *nuclein* that has a marked affinity for nuclear stain. This portion is supported by fine fibrils of *linin* that do not stain.

There is also present a semifluid substance known as the *karyoplasm* or *nuclear juice*.

The *nucleolus* lies within the nucleus and consists of a substance known as *pyrenin.* Just what is its function is not known. It probably has a distinct purpose during cell multiplication, as it disappears during the division of the nucleus, but reappears when the new nucleus is formed.

Another body, the *centrosome,* is also sometimes found. It is a small, highly refracting body, situated within the nucleus.

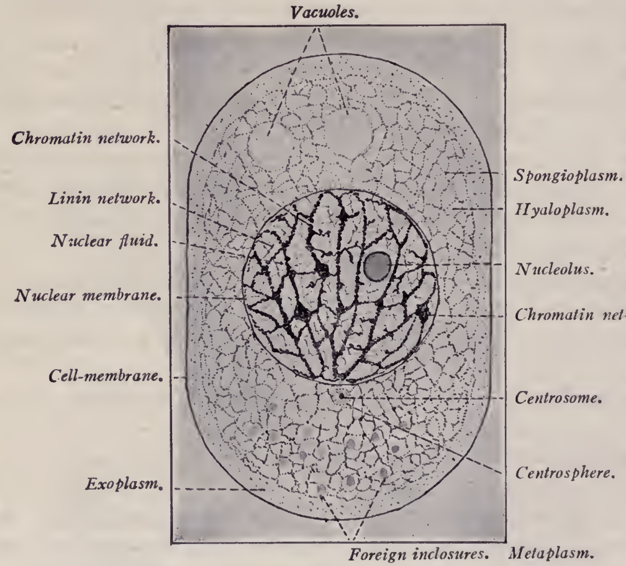


FIG. 15.—DIAGRAM OF A CELL (Huber).

It is surrounded by a clear area called the *attraction sphere.* This body, although it may be found during the stage of rest, becomes most noticeable during the stage of division of the nucleus. At that time it divides into two and passes to opposite poles of the cells.

Occasionally a small irregularly spheric body, the *paranucleus,* is present in the cytoplasm near the nucleus. Its function is not known.

The relation between the size of the nucleus and that of the cell varies greatly. In certain cells, as in the lymphocyte, the nucleus may occupy nearly the entire area.

The nuclei of the same kind of cells are usually similar in shape and size. They may be round, oval, or, as in some of the lower animals particularly, irregular. The shape of the cell depends partly on environment, partly on specialization.

A cell may also have one or more nuclei, the latter being known as *giant cells.*

With the exception of the red blood-corpuscles and the horny layer of the skin, all cells under normal conditions contain nuclei. The absence of a nucleus, therefore, usually denotes the loss of cellular activity.

The **functions of cells** which distinguish living from inorganic tissues can be divided into:

1. *Metabolism*, the power of selecting and assimilating food, anabolism; and the power of casting off excrementitious matter, catabolism.

2. *Growth*, the result of assimilation producing an increase in the size of the cell.

3. *Irritability*, response of the living cell to external influences.

4. *Motion*, which may be of three different kinds. There is a constant passage of a "circulating albumin" from one part of the cell to another. It may be *ameboid*, so called on account of its resemblance to the motion of the ameba. It consists of a streaming of the cytoplasm to one point, giving rise to prolongations or *pseudopodia* extending from the surface of the cell.

Ciliary movement is the result of the presence on the surface of cells of minute, hair-like processes, called *cilia.* These are prolongations and specializations of the protoplasm. The cilia keep up a movement like that of a whip-lash, always in the same direction.

5. *Reproduction* is the multiplication of a cell, and may take place in one or two ways, either by direct division, *amitosis*, which is not the common method, or by indirect division, *karyokinesis*, *karyomitosis*, or *mitosis.* The latter is the more usual way.

In *amitosis* or direct division there is first noticed a slight contraction in the nucleus of the cell. This gradually goes on until two new nuclei are formed. During this period the cytoplasm begins dividing, and by the time the nuclei have migrated to opposite poles, separation has taken place and two new cells have formed.

If the cytoplasm fails to divide, multinuclear or giant cells may arise.

Karyokinesis.—In *karyokinesis*, or indirect division, the cell goes through a very complicated course of changes of the various elements, probably the result of definite metabolic processes.

The changes can best be considered under four headings:

1. *The Prophase.*—The centrosome increases in size, passes from the nucleus into the cytoplasm, and divides into two.

Surrounding each centrosome is a mass of fine radiating lines known as the amphiaster. The rays extending from one centrosome to another are arranged in spindle form, the centrosomes being situated at the apices of the spindles. These achromatin rays form the nuclear spindle.

The nucleus has been enlarging and the chromatin increasing, its particles uniting to form a long fuzzy thread. These fibrils become tangled and convoluted and form the *close skein.* The fibrils become thicker, less convoluted, and arrange themselves in irregular loops, forming the *loose skein.* The chromatin now stains much more deeply than normally. These loops finally separate at their peripheral ends and form the *chromosomes*, **V**-shaped fibrils with their closed ends arranged in a clear space known as the *polar field.*

During the formation of the skeins the nucleolus and the nuclear membrane disappear and the chromatin fibrils lie in the cell protoplasm.

The chromosomes are always present in the same number in the same species, varying from 2 to 50 in various animals; in man being 24.

The arrangement of the fibrils about the polar field constitutes the *mother star* or *monaster.*

2. *The Metaphase.*—Each of the chromosomes undergoes a

longitudinal division into two. These filaments, with the closed end advancing, begin to separate, moving toward their respective poles or centrosomes.

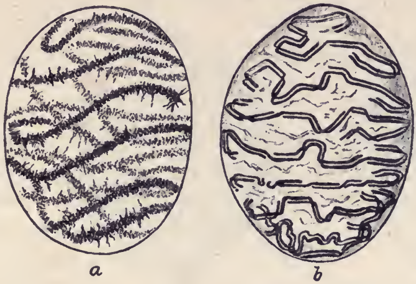


FIG. 16.—NUCLEAR CHANGES IN KARYOKINESIS (Hatschek).
a, Nucleus of spermatoblast of Salamandra maculata, with chromatin threads forming the first suggestion of a coil; *b*, close coil with disappearance of the fuzzy aspect and longitudinal cleavage of the threads.

FIG. 17.—DIAGRAMMATIC APPEARANCE OF THE RELATION OF THE CHROMOSOMES TO THE CENTROSOMES AND PRIMITIVE NUCLEAR SPINDLE (Flemming).

FIG. 18.—DIAGRAMMATIC REPRESENTATION OF THE NUCLEAR SPINDLE AND OF THE ARRANGEMENT OF THE DOUBLE CHROMOSOMES IN AN EQUATORIAL PLANE PREPARATORY TO SEPARATION. THIS STAGE IS CALLED THE MOTHER STAR (Flemming).

3. The *anaphase* begins with the migration of the chromosomes. As they move toward the opposite poles the free ends constitute the *equatorial plate*. Connecting the ends are

fine threads of achromatin known as the connecting filaments. The chromosomes collect at the opposite ends and form the *daughter stars* or *diasters*. As this occurs there is the beginning of a constriction of the protoplasm.

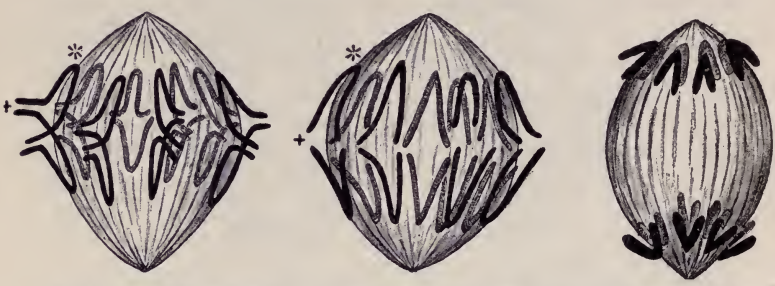


FIG. 19.—DIAGRAMMATIC REPRESENTATION OF THE SEPARATION OF THE CHROMOSOMES, WHICH ARE ATTACHED TOWARD OPPOSITE POLES OF THE NUCLEAR SPINDLE, ABOUT WHICH THEY GATHER TO FORM THE "DAUGHTER STARS" (Flemming).

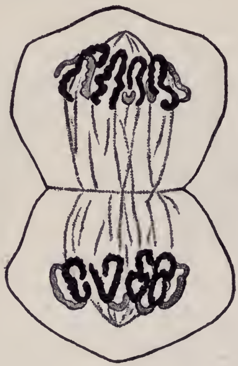


FIG. 20.—SEGMENTATION OF THE CYTOPLASM, AND THE CHROMOSOMES EQUALLY DIVIDED, ABOUT TO FORM NEW NUCLEI IN THE NEW CELLS (Flemming).

4. *The Telophase.*—The constriction continues until the original cell has been completely divided and two new ones formed. The chromosomes now undergo in reverse order the phases that have been described: the loose skein, the close

skein, the reappearance of the nuclear membrane and of the nucleolus, with finally the stage of rest.

To summarize, the changes are as follows:

Resting mother nucleus.

Prophase.

Migration and division of the centrosome with increase of chromatin.

Close skein.

Disappearance of the nuclear membrane.

Disappearance of the nucleolus.

Loose skein.

Separation of the skein into chromosomes.

Appearance of the polar field.

Rearrangement of the chromosomes around polar field.

Monaster, or mother star.

Appearance of the nuclear spindle.

Metaphase.

Longitudinal division of the chromosomes.

Anaphase.

Migration of the divided chromosomes to opposite ends of the cell.

Formation of the equatorial plate.

Diaster or daughter star.

Telophase.

Constriction of the protoplasm.

Daughter skeins undergoing in reverse order the above changes.

The stage of rest.

In some instances, instead of the cytoplasm dividing when cleavage of the nucleus is completed, it remains unchanged. This may go on until there are many nuclei, imbedded within a single mass of cytoplasm. Such formations are known as *giant cells*, and may be the result of division under unfavorable circumstances.

There may be the formation of more than two centrosomes with a resulting multipolar cell. The equatorial segments may split up more than once and the daughter cells may divide secondarily.

CHAPTER VII

INFLAMMATION AND REGENERATION

Inflammation is the protective reaction of irritated and damaged tissues which still retain vitality.

Etiology.—The causes of inflammation may be divided into *mechanical*, *chemical*, and *vital*, or *infectious* and *non-infectious*.

Traumatism of any nature, such as a blow or the action of chemicals, can give rise to an inflammatory reaction and be non-infectious.

The common cause, however, is the action of *bacteria* upon the tissues. The great majority, therefore, of inflammations are infectious or vital in variety.

A non-infectious one may become infectious through a secondary deposit of bacteria.

An infectious inflammation is distinguished by the fact that it is likely to be progressive, is capable of indefinite increase, and may also be transmitted from one individual to another.

Before taking up the pathologic changes of the circulation it will be necessary to first consider the normal differences in the blood-current in arteries, veins, and capillaries.

In *arteries* the stream is not constant; it is regularly intermittent on account of the rhythmic contractions of the heart. It is more rapid than in the veins; the red cells cannot be distinguished at the height of systole, but at the end of the heart's action the current slows sufficiently for them to be seen. The corpuscles occupy the entire lumen, except that at the end of the pulse-wave they momentarily withdraw from the wall of the blood-vessel.

In *veins* the stream is constant and is regular in speed. Instead of cells and plasma being uniformly mixed there are two zones present: an *axial* or central zone, composed of blood-cells, and a *peripheral* one, made up of the blood-plasma. In

this latter there are occasionally a few leukocytes, but no erythrocytes found.

In *capillaries* the current is neither constant nor regularly intermittent. It is constant during the flow.

The *changes in the circulation in inflammation* are as follows:

1. A momentary *contraction* of the blood-vessel following the introduction of the irritant. This is followed by:

2. A marked *dilatation* and *relaxation* of the vessel with at first an increase in the rapidity of the flow. Arterioles are first affected, then veins and capillaries.

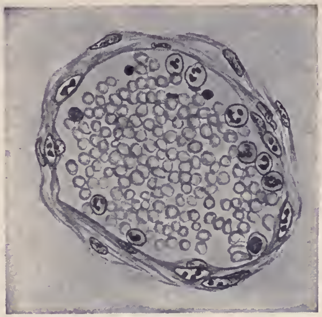


FIG. 21.—ACUTE INFLAMMATION (Mallory).

Peripheral arrangement of polymorphonuclear leukocytes in vein.

3. Further increase in dilatation with *slowing* of the current. Instead of the cells being unrecognizable in the arteries,

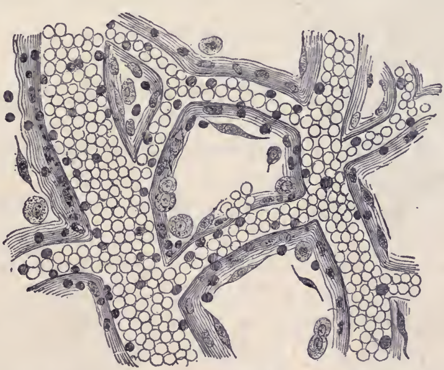


FIG. 22.—INFLAMMATION OF THE MESENTERY, SHOWING OVERFILLING OF THE BLOOD-VESSELS, WITH EMIGRATION OF LEUKOCYTES AND DIAPEDESIS OF RED CORPUSCLES (Ziegler).

they now become distinctly visible. Marked changes now occur, particularly in the venous circulation. The plasmatic

zone, which at first contained only a few leukocytes, shows an increase in their number until it is entirely filled with them. Subsequent to this there takes place an exudation of fluid and blood-cells from the vessels.

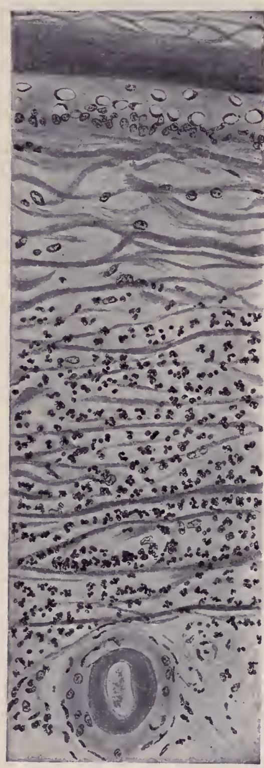


Fig. 23.—Acute Inflammation (Mallory).

Emigration and accumulation of polymorphonuclear leukocytes in the subcutaneous tissues of a rabbit's ear as the result of rubbing the surface with dilute croton oil.

Emigration or Transmigration of the Leukocytes.—At first the leukocytes adhere but slightly to the walls of the blood-vessel, assuming a pear shape, the enlarged ends pointing in the direction of the current. In the course of five or six hours all the small veins of the involved area may show a mass of leukocytes along their walls. These in time become closely attached, pass through the vessel walls, and, finally, may become *pus cells*.

As a rule, the greater number of leukocytes that escape are of the polymorphonuclear variety. They project a small mass of protoplasm through the vessel wall. This mass becomes gradually larger until the cell lies outside in the surrounding tissues. This process is known as emigration.

Diapedesis refers to the escape of red cells from vessels whose walls show no lesions.

At the same time that the cells escape there is an exudation or outflow of lymph through the vessel walls. This increased amount of lymph renders the tissue edematous and gives room for free ameboid movement of the leukocytes. Many are actively phagocytic, many

die, while some get back into the lymph-vessels and return to the general circulation.

As to the emigration of the leukocytes there are various theories, but the reasons are not perfectly understood. The phenomena can hardly be due to nervous influences, as the changes occur too slowly. It is also impossible to bring about an inflammatory reaction by stimulating either the vasoconstrictors or the vasodilators. When the latter is done, there is an exudation of plasma, but not of cells. According to Cohnheim, there is an increased permeability of the blood-vessel wall due to structural changes.

Probably the chief reason is that the ameboid motion of the leukocytes is very much stimulated.

It may also be the result of *positive chemotaxis*, the attraction that certain substances exert upon motile cells. Dead tissues and the products of bacterial growth are positively chemotactic, and their influence may be exerted upon the leukocytes while they are still within the blood-vessel.

Besides the polymorphonuclear leukocyte the round mononuclear form may also escape, giving rise to the *round-cell infiltration* that is found in subacute or chronic inflammation, particularly in tuberculosis and syphilis.

As a result of the disturbances of the circulation there are certain changes in the inflamed part as a whole that are frequently spoken of as the *cardinal symptoms* of inflammation:

Pain, or dolor, due probably to the pressure exerted upon the terminal nerve-filaments. Also to the action of toxins, acids, enzymes, etc., upon the nerve-endings.

Swelling, or tumor, due to the increased amount of blood present and to the exudate within the tissues.

Redness, or rubor, due also to the hyperemia. The increase of blood to the involved part brings more leukocytes, diluents, and antibodies, facilitates the removal of harmful substances, and possibly in some instances, affords increased nutrition to the cells in that area.

Heat, or calor, the result of two causes, one that more blood is brought to the part, the other that the blood moves more slowly and heat accumulates.

Altered function, or functio læso, may be added to the first four.

The products of inflammation are known as *inflammatory exudates.*

A *serous* exudate is one that is composed of fluid that has escaped from the vessels. It contains few cells, occurs in very slight inflammations, and tends to coagulate spontaneously.

This fluid differs from the non-inflammatory transudate in containing a greater amount of albumin, and, therefore, being of a greater specific gravity. The amount of exudate depends largely upon the vascularity of the part.

A *fibrinous* exudate is one in which there is more or less fibrin present, which probably helps restrict the escape of the infecting agents. It is formed by the action of fibrin ferment acting upon fibrinogen or fibrin-forming substances in the presence of calcium salts. This ferment is yielded probably to some extent by all the cells of the blood, but particularly by the leukocytes. When they die, the ferment is formed and the fibrinogen is converted into fibrin. When the leukocytes are increased in number, the amount of fibrin is usually greater.

A *purulent* exudate is one in which there is a preponderance of escaped leukocytes. It may be found infiltrating the tissues or in a circumscribed area known as an abscess. This exudate is known as pus.

A *hemorrhagic* exudation is one that contains erythrocytes. It generally indicates that there has been a lesion of blood-vessels.

Pus is an opaque, yellowish, alkaline fluid, specific gravity about 1050. It is made up of pus cells, either living or dead polymorphonuclear leukocytes, and *pus serum* (liquor puris). Usually some degenerated tissue cells are present. According to whether there is blood, serum, or mucus as well, it may be *sanious pus*, *seropus*, or *mucopus*.

If the fluid portion is scanty, the pus may be *creamy* or *cheesy;* or *ichorous* if the pus is very thin, watery, and acrid.

An *abscess* is a circumscribed collection of pus. It is sur-

rounded by an inflammatory zone incorrectly called a pyogenic membrane.

An abscess may be *hot* or *cold*. The first is the result of acute inflammatory changes. The latter is a chronic inflammatory process, and the fluid contained within it is not pus, but is made up of broken-down and degenerated tissues.

An *embolic* abscess is one that has followed the lodgment of a septic embolus.

Pyemic or *metastatic* abscesses are those resulting from pyogenic organisms present in the blood becoming lodged in the tissues and causing local purulent lesions.

The various steps occurring in the formation of an abscess due to bacterial infection are as follows: After the pus-produc-

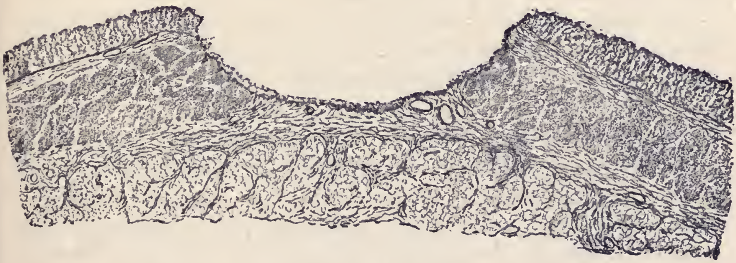


FIG. 24.—CHRONIC ULCER OF THE STOMACH, SHOWING A SECTION THROUGH THE STOMACH WALL AT THE CENTRAL PART OF THE ROUND ULCER (Delafield and Prudden).

ing organisms gain entrance they undergo multiplication without at first causing any reaction. In a very short time, however, the invaded area becomes congested, the leukocytes approach the wall of the blood-vessels, and degenerative changes in the neighboring tissue cells appear. There is a multiplication of the bacteria, the polymorphonuclear leukocytes escape from the vessels, and mononuclear leukocytes (small round cells) collect. The polynuclear leukocytes and other cells, including endothelial cells, take up large numbers of bacteria. More leukocytes appear until the tissue becomes

densely filled by them. This is accompanied by a yet greater proliferation of the bacteria which extend along the lymph-streams into the region outside of the developing abscess. There is now a breaking down of the leukocytes, with the setting free of various ferments and a coincident destruction of the tissue of the affected portion.

The destruction of tissue that accompanies abscess formation is in consequence of there being an insufficient amount of nutrition, and is due also to the dissolving effect of digestive enzymes present in the liquor puris, probably derived from the broken-down leukocytes.

When the broken-down tissue has been cast off there remains a superficial lesion with loss of substance. This area is known as an *ulcer*.

A *sinus* is an inflammatory tract that is open at one end from which the exudate can escape.

A *fistula* is an inflammatory tract that is open at both ends. It is one that joins an internal cavity to the surface.

The **termination of inflammation** depends upon the degree of inflammation and the amount of damage done. It may occur by *resolution*. This takes place only when the inflammation has been slight. The exudate is taken up by the lymphatics and returned to the circulation. Any degenerated cells will be taken up by the wandering leukocytes and the tissue will resume its normal condition.

In *suppuration* the inflammation has been destructive; there is actual loss of tissue, with the formation of pus.

As pus is formed it is either confined as an abscess or else it tends to infiltrate the tissues. In either case the tissues attempt to get rid of the irritating substance by having it follow along the least resistant paths and letting it escape from the body. This process of extension is known as "burrowing;" it results from the increased pressure due to the presence of the pus and to the digestive powers of the enzymes contained within.

In some cases the pus may quickly escape to the surface of the body and be cast off. It may, however, have to burrow a long distance, as in a psoas abscess, before it can escape.

Sometimes the pus may gain entrance into one of the cavities of the body, as the peritoneum or pleura, and give rise to inflammatory conditions there.

According to the cavity involved, the condition has special names. *Empyema* is pus within a pleural cavity; *pyopericardium* when within the pericardial sac; *pyosalpinx* when a Fallopian tube is involved, etc.

Encapsulation is what takes place when the irritating material cannot be removed from the body. The surrounding tissue cells undergo multiplication and the substance is isolated by the formation of a connective-tissue capsule about it.

Organization is the process of repair by means of which the destroyed areas are filled up by connective tissue. It is not a case of the transformation of the inflammatory products into connective tissue, but is a condition of replacing. This new formation of connective tissue is known as a *cicatrix* or *scar*, the process as *cicatrization.*

The cells present in the repair of inflammation are derived from various sources, and consequently differ among themselves.

The *leukocytes* that form the greatest numbers are derived from the blood and are chiefly of the polymorphonuclear variety.

Lymphocytes both large and small, as well as *eosinophiles* in small numbers, may also be present.

Eosinophile cells are actively ameboid and are able to escape from the blood-vessels. As a rule, they are not present in marked numbers except in certain subacute or chronic inflammations of the skin or mucous membranes.

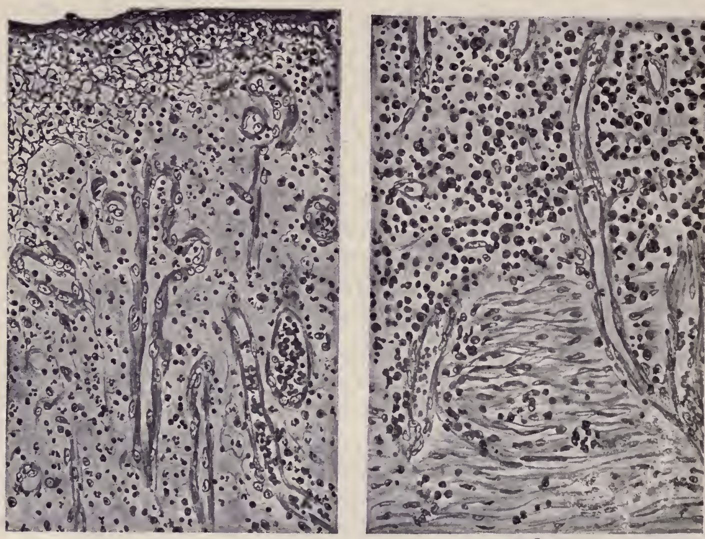
The *plasma* cells probably originate from the connective tissue, but may be derived partly from the blood. They are rather large, and contain a pale, vesicular nucleus eccentrically placed and a finely granular basophilic protoplasm. These cells are usually most numerous in acute toxic conditions and are supposed to play some part in the formation of connective tissue.

The *mast* cells or *basophilic leukocytes* are large cells containing usually a trilobed vesicular nucleus and large granules in

the cytoplasm. They are most common in inflammations of mucous membranes and in the neighborhood of tumors, especially if they have undergone mucoid changes.

The *fibroblasts* or *epithelioid* cells are formed by the proliferation of pre-existing connective-tissue cells.

Giant cells, those containing more than one nucleus, are frequently present. The formation of these cells probably



a *b*

FIG. 25.—GRANULATION TISSUE (Mallory).

a, Surface portion, composed chiefly of newly formed blood-vessels; very few fibroblasts; many polymorphonuclear leukocytes between the vessels and in the fibrin of the surface; blood-vessels and leukocytes separated by serum. *b*, Deeper portion; many lymphocytes between blood-vessels; young fibroblasts growing in horizontal arrangement at base.

takes place in one of two ways. If a single cell is not sufficiently powerful to remove the offending particle, several may coalesce, and in that way successfully make the attack. They may, however, form through a multiplication of the nuclei without division of the cytoplasm.

In the process of *repair* there is formed what is called *granu-*

lation tissue which acts as a strong barrier to absorption and infection. In it there is the formation of loops of new capillaries derived from the endothelial lining of pre-existing blood-vessels. The endothelial cell becomes larger, the nucleus divides by mitosis, and two cells are formed. These cells continue dividing until a sprout-like process extending into the surrounding tissue is formed. Adjoining sprouts unite, and, although at first solid, finally become hollowed out, thus allowing the circulation to be re-established. At the same time that this is taking place there is a multiplication of the *fixed* connective-tissue cells, which surround and act as a supporting framework to the loops of new-forming capillaries.

In the proliferation of the connective tissue there is first found a small round cell with a round or oval nucleus. As the tissue becomes older the cells tend to elongate and become spindle shaped. At first they are very close together, but gradually separate, and the homogeneous intercellular substance becomes fibrillar and supports the cells. Those cells concerned in the formation of the cicatrix are called *fibroblasts*.

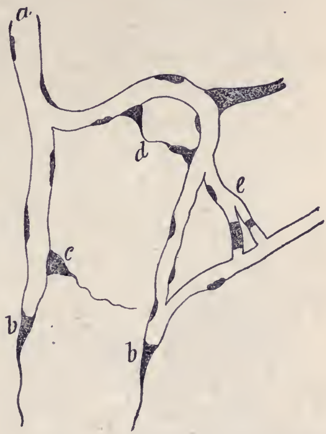


FIG. 26.—FORMATION OF NEW BLOOD-VESSELS, AS SEEN IN THE TAIL OF A TADPOLE (Arnold).

In the new-formed tissue there is at first an overproduction of cells and blood-vessels, but eventually it becomes less vascular and cellular. This is brought about to a great extent by the contraction of the cicatrix, which, at first reddish and elevated, finally becomes pale and depressed.

According to surgeons, cicatrization may take place in one of two ways:

Union by first intention, or *primary union*. In this the edges of the wound are closely brought together and very little exudate escapes. In this narrow space the same processes

take place as are seen in the formation of granulation tissue, coagulation, fibrin formation, phagocytosis, and proliferation of capillaries and connective tissue, but to a much less extent. The epithelial surface is replaced by a proliferation of the neighboring epithelium.

Union by second intention, *secondary union*, or *union by granulation*, takes place when the edges of the wound are far apart and there is a large amount of exudate present.

This process is the same as healing by first intention, except that in it there is supplied the material bridge over the gap.

If an epithelial surface is affected, the granulation tissue is gradually covered by proliferation of adjacent cells.

Regeneration, although commonly applied to the formation of cicatricial tissue, really refers to the power of individual tissues to reproduce their own kind.

Generally speaking, the more highly specialized the tissue, the less is its regenerative power. If such tissues are destroyed, they are generally replaced by fibrous tissue. A cell can give rise in regeneration only to a tissue that has the same blastodermic origin.

The *fibrous connective tissue* is probably the most active.

Epithelium of the surface variety is constantly and completely regenerating. Whether regeneration takes place in the more highly specialized epithelial organs, such as the kidney and liver, is rather improbable.

Muscular tissue is capable of regeneration to a slight degree, but the chief repair after injury to muscle takes place within the connective tissues surrounding the fibers.

Blood-vessels, as is seen in the formation of granulation tissue, are capable of marked multiplication. The new-formed vessels in regeneration are usually only temporary; existing only long enough for the tissue to receive its nutrition, then disappearing during the contraction of the cicatrix.

Bone, as is noticed in the repair of fractures, is able to undergo complete regeneration.

Cartilage is incapable of regeneration. In injuries it is replaced by fibrous connective tissue.

Nerve-cells of the highly specialized type, such as ganglion

cells, cannot regenerate, but the *neuroglia* or nerve connective tissue can. The neuroglia differs from the ordinary fibrous tissue in that it is derived from the ectodermic layer of the blastoderm.

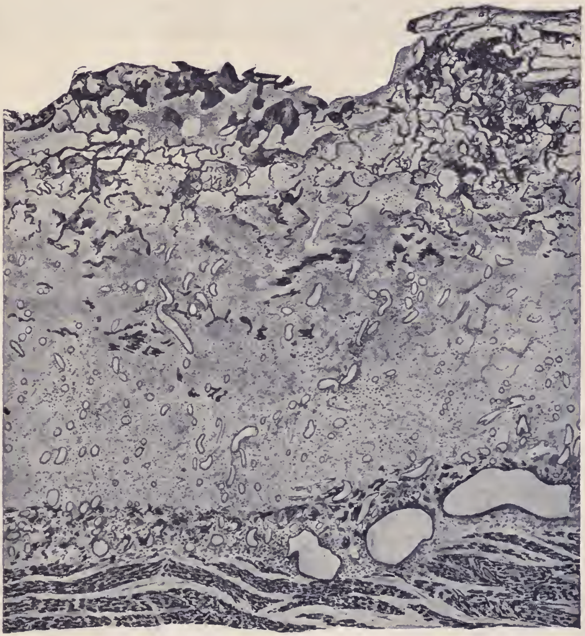


Fig. 27.—Heart. Organizing Pericarditis. Fibrin still Present Along Surface and Beneath it (Mallory).

Varieties of Inflammation.—Inflammation may be—

Acute when it arises rapidly, lasts a short time, and destroys tissue.

Chronic when arising slowly, lasting a long time, and giving rise to the formation of fibrous connective tissue.

Infectious when caused by some living organism.

Non-infectious when it does not arise from the action of a living organism.

Exudative if the inflammation is characterized by the presence of an exudate. According to the variety of the exudate, the inflammation may be as follows:

Serous when the exudate consists of a fluid having few cellular contents.

Fibrinous when particles of fibrin are present in the exudate.

Purulent when pus cells (leukocytes) are present in large numbers.

Hemorrhagic when erythrocytes escape in quantity.

Parenchymatous when the actively secreting cells of a glandular organ are involved.

Interstitial if the inflammatory process involves the connective-tissue framework of an organ.

Catarrhal when limited to mucous membranes.

In the early stage the secretion of mucus by the cells ceases, the surface becomes dry, and the blood-vessels congested. Later on, the secretion is increased in amount, frequently changed in character, and the congestion of the vessels somewhat lessened.

Desquamative if there is a casting off of epithelium in a catarrhal inflammation.

Vesicular when there are larger and smaller circumscribed elevated areas containing a serous exudate, as in blisters.

Pustular when the circumscribed elevations contain pus.

Diphtheric or *croupous* when there is a marked coagulation of fibrin on the surface with the formation of a pseudomembrane in which are found degenerated cells of various types—epithelial, leukocytes, and erythrocytes.

In it there is usually necrosis involving the superficial epithelium, or going deeper and attacking the submucosa as well as the mucosa.

Ulcerative if accompanied by a loss of superficial substance.

Degenerative when the destruction of tissue is extensive.

Adhesive when, as the result of the presence of fibrin, replacement by fibrous tissue follows and the two opposing surfaces become more or less adherent, the process being the same as occurs in scar formation. It may go on to the point where the cavity entirely disappears, and is then called *obliterative.*

Gangrenous when there has been infection of the tissues by putrefying, saprophytic organisms and gangrene is present.

Phlegmonous when the interstitial tissues become infiltrated by pus.

Productive when the formation of fibrous connective tissue is prominent.

Specific when caused by a definite micro-organism.

CHAPTER VIII

THE SPECIFIC INFLAMMATIONS (GRANULOMATA)

TUBERCULOSIS

Tuberculosis is a specific infectious disease characterized by the formation of tubercles.

It is caused by the Bacillus tuberculosis, which is non-motile, non-sporogenous, aërobic, acid resisting, and purely parasitic. Occurs as a slender, rod-shaped, slightly curved body, usually with rounded ends, but sometimes showing distinct branches. It is about 1.5 to 3.5μ long by 0.25μ wide. It is found in sputa and in the lesion of tuberculosis. It is the cause of all forms of tuberculosis in man and may be transmitted to many of the lower animals. It is still unsettled whether the forms found in animals are capable of being pathogenic to man. The bovine bacillus, however, is apparently pathogenic in a small percentage of cases.

Staining is difficult, but after having once taken it up, the organism is with difficulty decolorized. Use Ziehl-Neelson method. Stains by Gram's.

Culture.—Blood-serum, glycerin agar-agar, potato, and glycerin bouillon. It is difficult to cultivate, growth is slow, best at 37° C., none when below 29° C. or above 42° C. Growth is dry, lusterless, coarsely granular, wrinkled, and slightly yellowish.

Pathogenesis.—Tuberculosis results from the successful invasion of the Bacillus tuberculosis. This may take place by means of: (1) the respiration; (2) the blood circulation; (3) lymphatic channels; (4) ingestion. After having gained entrance it may give metastases by and of the first three, by continuity of tissue, or by direct implantation.

The characteristic lesion is the miliary tubercle, which is gray in color as long as degeneration and caseation have not

occurred; it then becomes yellow. It is rarely circumscribed by any definite boundary, and it tends to infiltrate and form tubercles in the adjacent tissues. It is a small area of inflammation and degeneration resulting from the action of the bacillus. The primary lesion does not necessarily occur at the point where the bacilli gained entrance. When the organism enters a suitable location, it undergoes multiplication. In a short time their number and the products of their metabolism

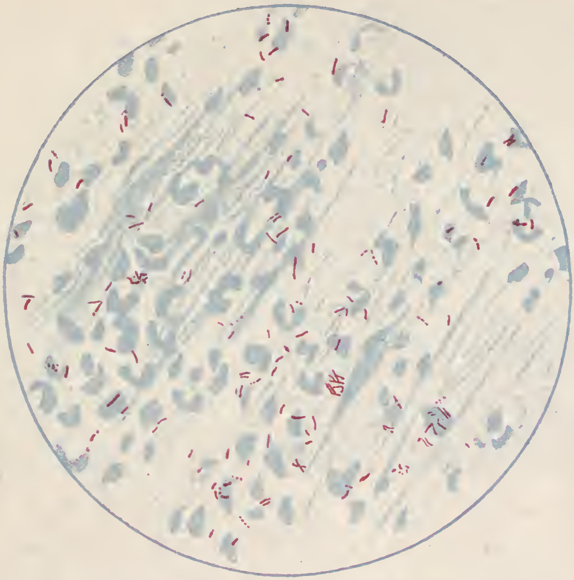


FIG. 28.—BACILLUS TUBERCULOSIS IN SPUTUM, ZIEHL-GABBETT. × 650 (Cornet and Meyer).

bring about an increase in the number of fixed connective-tissue cells—epithelioid cells. These cells are the first to appear. A little later, through the chemotactic effect of the bacteria, lymphoid cells escape from the blood-vessels. According to which cell predominates, the tubercle may be either *epithelioid* or *lymphoid*.

As the bacteria multiply, more nutrition is required, but

this variety of inflammation is peculiar in that not only no new blood-vessels are formed, but the pre-existing ones are destroyed by endarteritis and thrombosis as the process advances. Consequently, the central area, the older portion, undergoes degeneration and coagulation necrosis.

The tubercle may be divided into three zones, according to its histologic characteristics: (1) A *central* zone containing bacteria and tissue cells that have undergone coagulation

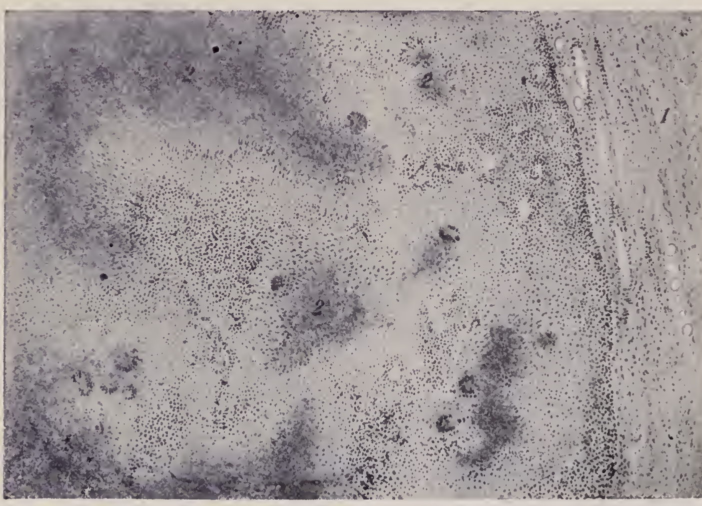


FIG. 29.—SUBACUTE TUBERCULOSIS OF a LYMPH-GLAND. × 70 (Dürck)
1, Thickened capsule; 2, caseous centers of the tubercles. At the periphery of the gland the tubercles are still discrete, and between them lies lymphadenoid tissue. In the center of the gland the nodules have formed larger confluent areas. Numerous giant cells.

necrosis. (2) A *median* zone, in which are many epithelioid cells and frequently giant cells containing vesicular nuclei arranged peripherally and radially. (3) A *peripheral* zone, in which are found a few epithelioid, many lymphoid, and some plasma cells.

The giant cells as well as the epithelioid may come from the endothelium of the blood-vessels or lymph-vessels, from fibroblasts or from escaped leukocytes.

If the process has been rapid, the lymphoid cells usually predominate. If the individual's resistance is fairly good, some of the epithelioid cells may be converted into fibrous tissue. When resistance is marked, the tubercle may become encapsulated by fibrous tissue, and eventually become infiltrated by lime salts. This occurs only where the resisting power of the patient becomes greater than the destroying ability of the organism.

As, however, the bacilli keep continually multiplying, the tendency of the disease is to extend. This occurs by the organisms beings carried into the lymphatic channels either directly or by the action of phagocytes. The latter may carry and deposit them in a neighboring lymph-node, where secondary lesions will occur. Metastasis may also take place by the organisms gaining entrance into a vein, entering the general circulation, and setting up a more or less widely diffused general miliary infection.

Recovery from tuberculosis is more common than is generally believed. According to post-mortem examinations, 20 per cent. of the cases of tuberculosis recover. In such cases there is present the ability of the individual to resist the inroads of the process. The tubercle bacilli become encapsulated in a mass of connective tissue that prevents their further growth and extension. This new-formed tissue tends to contract and causes the broken-down portions to be absorbed, or else calcareous infiltration takes place.

These walled-off areas are, however, still a source of danger. Although tubercle bacilli do not form spores, yet infection may take place years after the connective-tissue growth, if for any reason the contents happen to escape.

When it remains quiet it is called "latent" tuberculosis.

The symptoms seen are probably due in a great part to the presence of associated pyogenic organisms. The night-sweats, fever, and loss of weight seen in cases of pulmonary tuberculosis are due to the associated bacteria. There is generally present some anemia, and many authors claim that there is an increase in the number of lymphocytes in the blood.

The liver frequently shows marked fatty infiltration and

sometimes amyloid degeneration to a slight or a marked dcgree, depending upon the amount of suppuration.

The most common entrance for infection is the respiratory system. Sputum from tuberculous patients becomes dried and comminuted; it is then carried about by the currents of air and enters the body.

The intestines may become secondarily involved through infection brought about by swallowing the tuberculous sputum.

Congenital tuberculosis may come from the paternal side from infection of the genitals; from the maternal side through infection of an ovum, or it may be transmitted through the placenta. Heredity is no longer thought to have much direct influence. It is now believed that what is inherited is nothing more than a weakened resisting power.

Fig. 30.—Giant Cell from a Leprous Ulcer of the Epiglottis, Showing the Lepra Bacilli Scattered Through the Tissue and Enclosed in a Large "Lepra Cell" (Lehmann and Neumann).

LEPROSY

Leprosy is a chronic, specific, infectious, inflammatory disease caused by the Bacillus lepræ, which is a non-motile, non-sporogenous, acid-resisting, purely parasitic organism. It is pathogenic for man, but some of the lower animals appear to be somewhat susceptible. Is very slightly contagious. Is stained with some difficulty. Stains by Gram's. An acidfast organism supposed to be the B. lepræ has been grown on artificial culture-media containing split-up nucleoproteins.

It occurs most commonly in warm climates and in people of almost any age. Is most common in males of from twenty to thirty years. It is probably not hereditary, but children under three years have been affected. Infection may be transmitted by: (1) direct inoculation; (2) kissing and sexual intercourse; (3) clothing; (4) bites of insects.

The bacilli are distributed to an extraordinary extent in

the body of the leper, and in many cases there will be no inflammatory reaction in their neighborhood. They may be either extracellular or intracellular, and in the latter case may be found in giant cells or lepra cells. These may contain numerous nuclei and numbers of vacuoles as well as bacteria.

The secretions of the numerous membranes of the nose usually contain great numbers of the bacilli.

FIG. 31.—NODULAR LEPROSY.

Varieties.—Two forms are commonly met with, the *nodular* and the *anesthetic* or *nerve* leprosy. It is seldom, however, that a quite pure case of either is found; the majority belong to the mixed form. In the *nodular* variety the node may be preceded by a hyperemic patch which leaves behind it a pigmented area. The nodules appear first in the skin and subcutaneous tissue of the face, and may remain single or become confluent.

Macroscopically the nodes are rather grayish or yellowish.

Microscopically each node is made up of granulomatous tissue composed of lymphoid and epithelioid cells retained in a loose connective-tissue network; in these masses the bacilli occur in great number between and in the cells. These lesions are more vascular than those of tuberculosis, and consequently do not tend to undergo coagulation necrosis. Caseation does

FIG. 32.—MACULAR LESIONS IN ANESTHETIC LEPROSY.

not take place and the ulceration that is so common depends largely upon injuries and secondary infections.

The nodules are found in other parts of the body, as on the back of the hand,—palm is not usually involved,—in the mucous membrane of the eye, nose, mouth, larynx, and intestines.

The lymph-glands in both varieties are swollen, hard from

connective-tissue formation, and yellowish on account of fatty degeneration.

Anesthetic leprosy is characterized by the growth of the bacilli in the sheath of the nerves and an increase in the connective tissue along their course. Is most common on the ulnar and popliteal nerves, which at first may be painful. There then appears neuritis with localized hyperemic spots, the nerve affected being red and swollen; later it becomes harder, pale, and gray, with nodular or fusiform enlargements. The neurilemma usually becomes thickened, fibrous, and infiltrated by cells and bacilli. These become anesthetic, and in some cases become the seat of a blister. Finally, ulceration may develop with the subsequent loss of the fingers or toes.

Many of the enlarged nodes may be the result of a secondary tuberculosis occurring late in the course of the disease. There is frequently fever and also nephritis. Amyloid degeneration is not uncommon in the ulcerative forms.

The majority of the cases last from five to twenty years, usually dying of tuberculosis.

GLANDERS

Is a specific infectious disease of horses that is sometimes seen in man as the result of accidental infection.

Is caused by the Bacillus mallei, a non-motile, non-sporulating, aërobic or optionally anaërobic bacillus 2 to 5 μ in length. Is pathogenic for man and lower animals. Stains by ordinary methods, but not by Gram's. Grows on ordinary media, but best on glycerin agar.

It makes its appearance in the membrane of the nose in horses in the form of small nodules the size of a pea. These may increase in size, but eventually break down and ulcerate, with the formation of irregular ulcers, having yellowish, elevated, and indurated borders from which some bloody pus is discharged. Lymph-nodes become enlarged, and metastatic abscesses may result. The lungs are frequently involved and macroscopically resemble a tuberculous bronchopneumonia.

Microscopically the nodules consist of masses of small round cells and epithelioid cells. Do not find giant cells.

If the skin is involved the condition is known as "farcy," and the nodules as "farcy buds." They generally undergo central necrosis and suppuration with very extensive ulceration.

Man may become infected through lesions of the mucous

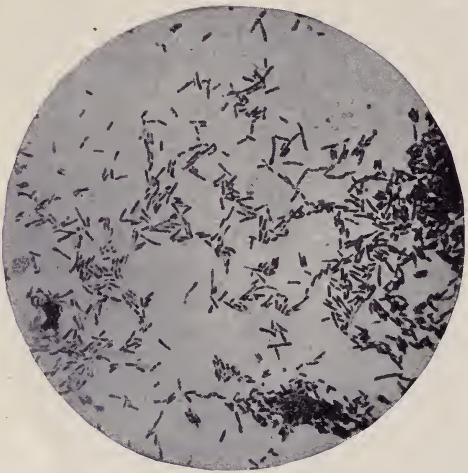


FIG. 33.—BACILLUS MALLEI, FROM A CULTURE UPON GLYCERIN AGAR-AGAR. × 1000 (Fränkel and Pfeiffer).

membranes of the eye or nose or of the skin, and the result is usually fatal. The course is that of an acute febrile affection suggesting typhoid fever.

SPOROTRICHOSIS

Is a chronic inflammatory process due to the presence of a pathogenic fungus, formed of sporangia and mycelia, the *sporotrichium*. These organisms are strictly aërobic; grow on the ordinary culture-media at a temperature of 20° to 28° C. They do not stain well, taking the ordinary anilin dyes faintly; if not decolorized too vigorously they stain by Gram's method.

The lesion quite commonly starts at the site of some trifling injury, particularly of the hand. The infected area may or may not become sluggishly inflamed, and there develops a small

dermic, sometimes subcutaneous, nodule which may break down and become soft. This may develop into a sluggishly inflamed, discharging sore.

Sooner or later a subcutaneous nodule will be felt at the lower end of the forearm. This gradually enlarges to the size of a cherry, may spread laterally, and finally softens. The overlying skin becomes thinned and of a purplish color, then breaks through, the discharge being of a viscid, gelatinous, seropurulent character. This formation is successively followed by several such nodules higher up the arm along the lymphatic vessels which can be felt usually as hard cords.

Microscopically may conform more or less closely to one of three types, or there may be an admixture of all varieties: 1. Proliferation of the connective tissue with lymphoid cells, syphiloid. 2. Epithelioid proliferation with giant cells, tuberculoid. 3. Polynuclear infiltration resembling suppuration.

It may be difficult to find the organism by staining the discharges, but the fungus grows readily on ordinary culture-media.

ACTINOMYCOSIS

Is a chronic contagious disease of cattle, "lumpy jaw," but is sometimes found in man.

Is caused by a fungus, probably a streptothrix, the *Actinomyces bovis*, which is large enough to be seen by the naked eye, appearing as small yellow particles. The fungus is made up of a central mass of granular substance in which there are many structures resembling chains of cocci or spores. Extending from this center are many mycelial threads terminating in club-shaped extremities. Is both aërobic and anaërobic in its growth; was formerly thought that the latter form alone was pathogenic. Will grow on any artificial media.

Stains yellow with picric acid, red with picrocarmin, blue with anilin gentian and by Gram's.

The infection is supposed to take place by means of spores gaining entrance into the human system by means of food or by inhalation. Probably enters by way of decayed teeth or through abrasions of the mucous membrane.

Where the fungus lodges there is a formation of nodules which break down, form abscesses, and discharge a creamy pus containing yellowish granules; which show the characteristic rayed appearance when looked at under the microscope.

The neighboring bones may become riddled with sinuses and there may also be metastatic growths in other organs, particularly the lungs. In the latter extensive necrosis may occur, with the formation of small cavities containing pus and fragments of degenerated tissues, and the fungus will be found in the sputum.

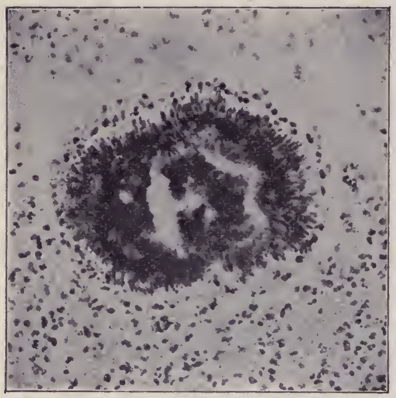


Fig. 34.—Actinomyces Cluster Showing Radial Striations at Periphery (Karg and Schmorl).

Instead of breaking down, connective tissue may be formed and encapsulate the invaded area.

Microscopically there is found a granulation tissue containing large masses of lymphoid cells, a few epithelioid cells, and giant cells resembling closely a tubercle.

MYCETOMA

Mycetoma or *Madura foot* is a chronic specific inflammatory condition caused by the *Actinomyces maduræ.* This organism closely resembles the A. bovis, but the club-shaped extremities are absent and spores may occur along the threads. Can be grown artificially; stains by the ordinary methods and by Gram's.

Usually attacks but one foot, particularly the great toe, but may involve the leg, arm, or hand. A nodule slowly appears, and in the course of a year or two may soften and discharge a thin pus in which are found minute rounded bodies resembling

fish-roe. These bodies may be either pinkish in color, the *pale*, or *ochroid* variety, or black like gunpowder, the *melanoid* form.

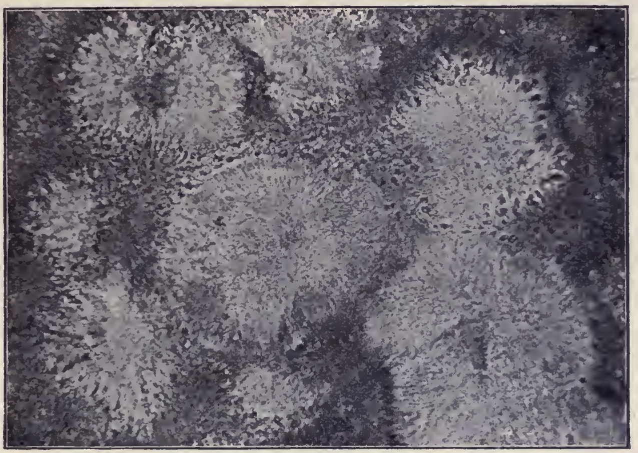


FIG. 35.—ACTINOMYCES OF MADURA FOOT (Wright and Brown). Granule crushed beneath a cover-glass, showing radial striations in the hyaline masses. Preparation not stained; low magnifying power.

On account of the degeneration numerous sinuses may form. The disease is painless and seldom fatal.

SYPHILIS

Is a specific, infectious, and very contagious disease of man. By experimental inoculation it has been transmitted to the higher apes and rabbits.

Is due to the *Treponema pallidum* (*Spirochæta pallida*), an organism that has been so constantly found in syphilitic lesions that it seems most probable that it is the causative factor. This organism is long, actively motile, spiral or corkscrew in shape, and with pointed ends. It is from 4 to 20 μ long, 0.25 μ thick, and contains six to fourteen turns which are short, clear cut and regular. It is difficult to stain and to grow, but it has been obtained in pure culture.

The disease may be divided into the—

1. Period of primary incubation, about three weeks.
2. Period of primary symptoms, chancre and adenitis.

Fig. 36.—Section from a Primary Syphilitic Nodule of the Mucous Membrane of the Mouth, Showing Collections of Cells About the Blood-vessels in the Submucous Tissue (Delafield and Prudden).

3. Period of secondary incubation, about six weeks.
4. Period of secondary symptoms, from one to three years.

5. Intermediate period of two to four years, during which the patient may recover.

6. Period of tertiary symptoms, unlimited.

The **primary lesion** is the *chancre*, which starts as a single papule, seldom multiple, at the seat of inoculation, which may be either *genital* or *extragenital*, and is invariably present except in congenital syphilis. This soon becomes eroded as a result of superficial necrosis, but increases in size due to infiltration of the deeper tissues. Is circular or oval, 1 by 1.5 cm., base hard. The edges are sharply defined, the induration not extending much beyond the lesion, and terminating abruptly. The chancre is slightly elevated and movable, not being adherent to the underlying tissues. Secretion is thin and scanty, suppuration being unusual; the surface may be dry or covered by a slight false membrane.

Microscopically there is a tremendous infiltration of cells, particularly in the neighborhood of the vessels, and marked changes in the walls of the blood-vessels. The infiltration begins with an escape of small round lymphoid cells, and this is accompanied by a proliferation of the cells of the cutaneous connective tissue and the cells of the walls of the blood-vessels. The elastic tissue disappears, the new formation of cells extending along the small arteries and veins. The tissue becomes crowded with various kinds of cells—polymorphonuclear leukocytes, lymphocytes, plasma cells, endothelial and connective-tissue cells, and fibroblasts. The media of the vessels thickens, the endothelium of the intima proliferates, and the lumen may be partially or completely obstructed. As a result of the interference with the circulation degeneration begins. The vessels not infrequently show hyaline changes.

Secondary Lesions.—From the time the chancre begins to form the spread of the disease begins by invasion of the lymphatics. By the time the chancre is well developed enlargement of the neighboring lymph-nodes can be observed. This continues even after the chancre has disappeared, and the enlarged nodes are found to be hard, free from inflammation, painless, and movable. They also do not suppurate. The nodes most commonly involved are the postcervical, sternomastoid, sub-

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maxillary, epitrochlear, axillary, and inguinal. Enlargement of the epitrochlear is particularly suspicious, as it is seldom attacked except in syphilis.

There then appear skin eruptions, polymorphic in character, accompanied by fever, constitutional symptoms, and a rapid decrease in the erythrocytes, with a moderate leukocytosis, usually of the lymphocytes. The skin lesions are generally symmetric, do not itch, and are coppery in appearance. May be some loss of hair, due to inflammation of the hair-follicles. The patches are irregular and have a "moth-eaten" appearance.

The *mucous patch* or *condyloma latum* appears on the mucous membrane and the contiguous skin surfaces, particularly those that are naturally warm and moist. It is a slightly elevated, moist, grayish lesion, covered by a thin pseudomembrane. In

Fig. 37.—Upper Median Incisors in Hereditary Syphilis (Cornil and Ranvier).

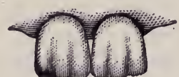

Fig. 38.—Serrations in Normal Teeth (Cornil and Ranvier).

these there is round-cell infiltration of the skin, with superficial necrosis and edema. There may be one or more patches.

Although the chancre and the secondary lesions are highly contagious, the mucous patch is probably the most so.

The chief tertiary lesion is the *gumma*. It is found most commonly in the nose and nasal septum, scalp, iris, shoulders, arms, and internal organs. The gumma develops as a nodular mass composed of great numbers of embryonic connective tissue and lymphoid cells with a very small amount of trabeculæ. Blood-vessels, most of them showing thickening of their walls, are numerous and may be found even during necrotic changes of the tissues. This would indicate that the breaking down processes are probably due largely to the syphilitic poison and not to obstruction of the vessels. It usually undergoes a caseous or other form of degeneration, with ulceration or absorption and subsequent cicatrization. It is hard, dense, and elastic.

When the growth of the gumma ceases, the younger peripheral cells become organized into connective-tissue cells, forming an envelope for the cheesy and gummatous center. This envelope shrinks, the semifluid portions are absorbed, and finally a scar, possibly calcareous, is left.

The blood-vessels show an endarteritis which closes or narrows the lumen. The remains of broken-down cells and particles of fat are present, and giant cells may be found. As the Treponema pallida have been found in gummata, and inoculations into apes have caused syphilis, the tertiary lesions must be considered infectious.

Congenital syphilis may result from disease of the ovum, spermatozoön, or both, or it may be transmitted through the placenta after conception has taken place, this being the most probable.

The mother, although showing no signs of syphilis, cannot be infected by nursing her child that is suffering from the disease (Colles' law).

Whether this immunity is real or whether the mother acquires it by being herself affected, although so lightly as to cause none of the usual symptoms, is still an unsettled question. As the Wassermann reaction is generally positive with the mother's serum, it would seem that she is usually infected.

An apparently healthy baby born of a syphilitic mother cannot be infected by her (Profeta's law). This apparent immunity may indicate that the child has received a true but latent infection, one that may not make its appearance until later in life.

The fetus may die *in utero* and be aborted, the child may be born dead, or it may be alive, but die shortly after birth.

The primary lesion does not occur in the hereditary form, but the secondary and tertiary manifestations may be evident, such as skin eruptions and mucous patches or even gummata. The characteristic lesion of congenital syphilis is pemphigus. There are present on the palms or the soles blister-like elevations of the skin containing a bloody or a greenish fluid.

The upper incisors of the second dentition are frequently

conical and peg shaped, with deep notches at the free edge (Hutchinson's teeth).

There also frequently occurs a "white" pneumonia, cirrhosis of the liver, spleen, and pancreas, osteochondritis, and interstitial keratitis.

CHAPTER IX

PROGRESSIVE TISSUE CHANGES

HYPERTROPHY

HYPERTROPHY, generally speaking, means an enlargement or overgrowth of any kind. It is usually divided into *true* and *false* hypertrophy, or *hyperplasia*, as the latter is called.

True hypertrophy is a uniform enlargement of a part, dependent upon an increase in size of all of its component elements. Accompanying the enlargement there is an increase in the functional power of the part involved.

The hypertrophy may be either *congenital* or *acquired*. It may also be either *physiologic* or *pathologic*. The former, however, may come under the latter heading when it reaches a degree that is not normal to the individual.

Hypertrophy is called *compensatory* when one organ takes upon itself the amount of work that was primarily carried on by two; is known as *vicarious* when another function increases at the expense of one that has been destroyed.

Etiology.—1. *Congenital causes*, in which case there are marked overgrowths of portions of the body, especially of the fingers and toes.

2. *Exercise* calls for an increased amount of energy. This demand is met by a greater supply of food with a subsequent increase in size, and is seen in the enlarged muscles of a blacksmith, or in a kidney when the other one is diseased or absent. This latter is an example of *compensatory* hypertrophy.

3. *Nervous influences* in some indefinite way play a part in hypertrophy, as is seen in the enlargement and increased function of the mammary glands during pregnancy.

4. *Disease of the hypophysis cerebri* apparently causes the condition called *acromegaly*, in which the tissues of the face and extremities hypertrophy.

Morbid Anatomy.—The part affected is uniformly increased in size.

Microscopically hypertrophy may be divided into the *simple* or *true* and the *numeric* (hyperplasia).

In the *simple* there is an increase in the size of the individual cell. This is seen particularly in the pregnant uterus, where at term the unstriped muscle cells may be eleven times as long and four times as broad as normal.

In the *numeric* variety the cells increase in number, but not necessarily in size; may even be smaller than normal.

Hyperplasia, or **false hypertrophy,** is a condition in which there is an increase in number of the cells with usually an asymmetric enlargement of the tissue. It is an excess of one constituent of an organ without a corresponding growth of the other elements.

The fibrous connective tissue is most commonly involved.

Etiology.—1. *Irritation* is the most common cause, if not too severe in character. In that case inflammation with consequent degeneration results.

The irritation may be *mechanical*, such as results from intermittent pressure exerted by tight shoes, or from the presence of a foreign body. *Chemical* irritants, such as alcohol, will bring about an increase in the amount of connective tissue, particularly in the liver, in which case there is also an increase in the number of bile capillaries.

2. *Nervous influences*, such as bring about the condition known as pseudohypertrophic muscular paralysis. In it there is not an increase in the muscle itself, but the fat has undergone a hyperplasia. There is also a fatty degeneration, with atrophy of muscle-fibers.

3. *Compensatory*, such as occurs when, on account of the decrease in size of an organ, the surrounding tissues have undergone a hyperplasia in order to supply the deficiency.

Morbid Anatomy.—The part involved may be much larger than normal or, on account of the contraction of the newly formed connective tissue, be much smaller. In either case the change is not symmetric.

In elephantiasis the part involved will be irregularly enlarged

as a result of the obstruction of the lymphatics and the increase in the number of cells.

In hyperplasia of the connective tissue of the liver the organ may be smaller than normal and have a roughly granular surface.

Metaplasia refers to the transformation of one tissue into one of another variety. The new variety must, however, be one derived from the same blastodermic layer. There is not, however, a development of less specialized tissues into a higher type; a simple epithelium cannot, in the vertebrates, give rise to a more complex glandular tissue or to nerve-cells. Columnar epithelium may become converted into stratified squamous epithelium with keratosis, as in the uterus, gall-bladder, or larnyx. This change is more common in the connective-tissue group, as in the formation of fat from areolar tissue, of bone from fibrous tissue, etc.

Heteroplasia is the development of a new tissue in a locality where it is not normally found. This is seen particularly in connection with neoplasms.

Anaplasia refers to the reversion of a cell to a less specialized stage. It is a change occurring preparatory to an increased proliferation. Is applied mainly to tumor formation. Hansemann's studies of tumor cells show that unequal, asymmetric and multipolar mitosis, and destruction of chromosomes is of frequent occurrence, especially in the more malignant tumors. The term "anaplasia" is applied to these cells, signifying a loss of normal differentiation, of specific function, and of organization.

Anaplastic cells are, therefore, not embryonal cells, but a new type which has lost its place in the old organization.

CHAPTER X

TUMORS OR NEOPLASMS

A *tumor* is an abnormal mass of cells or tissues resembling those normally present, but arranged atypically. It grows without any definite limit at the expense of the organism, without serving any useful function.

The cause of such growths is as yet unknown. They are made up of tissues that have their counterpart either in the embryonal or adult development. They differ in having a more or less atypical arrangement, in occurring in tissues in which they are heterologous, and in not having any mechanism to control their growth and function. Inflammation is unessential to their occurrence, and their structure is dissimilar to that of inflammatory lesions. There is no hyperemia, no exudation, no leukocytic invasion, no granulation tissue, no cicatrization. Tumors tend to increase and persist, while most inflammations tend to recover and disappear. Inflammatory growths always consist of connective tissue, regardless of the tissue or organ in which they occur.

Theories of Origin.—They are numerous, but as yet no one answers in every case.

1. *Spermatic Influence.*—It was thought that the normal tissue where the growth occurred had become directly transformed into the tissue of the tumor, but this is not in any way supported.

2. *Mechanical Irritation Theory of Virchow.*—By this it is claimed that new growths arise in tissues that have been the seat of injury or chronic irritation. Such cases as the development of epitheliomata on the lower lips of pipe-smokers, carcinoma of the gall-bladder associated with gall-stones, scrotal cancer in chimney-sweeps, *x*-ray cancer, cancer of mouth in Ceylon, Kangri cancer in natives of Kashmir, etc., would seem

to uphold this theory. It is probable, however, that the injuries and irritation are not the causative, but are predisposing, factors.

3. *Theory of Embryonic Remnants* (Cohnheim).—The author of this theory believed that "in an early stage of embryonic development more cells were produced than were required for the formation of the tissue involved, so that there remained unused a number of cells, possibly very few, which, on account of their embryonic character, were endowed with the power of marked proliferation." These remnants are frequently spoken of as "rests." Cohnheim thought that they could lie latent for many years and develop in after-life if conditions should become favorable. No explanation is given, however, as to what is meant by "favorable conditions."

Such groups of cells have been observed not infrequently in various tissues and organs of the body. Adrenal rests are not uncommon. In certain forms of tumors this theory seems to hold good: in enchondromata of the testis and parotid glands and of other organs, and particularly in the case of the dermoid cysts.

4. *Parasitic or Infective Theory.*—It has been claimed by many investigators, especially concerning the carcinomata and sarcomata, that tumors are caused by the presence of living micro-organisms. Bacteria were first supposed to be the cause, but protozoa and blastomycetes have also been suspected. The general opinion, however, is that these cell inclusions are portions of broken-down nuclei or else secretions of the cells. Attempts to grow these bodies have, as a rule, resulted in failures, or, if grown, have not reproduced the disease in other animals. Up to the present no specific micro-organism has been demonstrated in cancer or in any other spontaneous new growth. Attempts to transplant human carcinoma from one person to another have not as yet been successful, although transplants of tumors have been made in many generations of mice and rats. Success occurs only when the growth has been implanted in other animals of similar kind. Such experiments, nevertheless, do not show the necessity of any low form of organism. It is well known that portions of skin can be

transplanted from one person to another. More recently attempts have been successful in causing sarcoma-like tumors to grow in hens that have been inoculated with a filtered extract of the growth.

5. *Theory of Decreased Tissue Resistance.*—Ribbert's theory is that the connective tissue loses its normal resisting power or "tissue tension," and by doing so allows the epithelial cells to undergo abnormal proliferation. The essential feature is that the cells must become separated from their normal relation to the surrounding tissue and then take on an active growth.

This theory is not satisfactory, as in the healing of wounds scattered groups of epithelial cells are found constantly which have actively pushed over and into the underlying granulation tissue, yet tumor formation in such cases is exceptional.

6. *Nervous Theory.*—This was to the effect that through disturbances of the trophic nerves the tissues were able to undergo an overgrowth. Certain investigators have shown what seems to be a definite correspondence between the occurrence of skin cancer and the distribution of certain cutaneous nerves.

Of other theories, that of Adami is interesting. According to him the cell, instead of adhering to the habit of function, has reverted to an earlier stage, one in which the habit of growth predominates. The energy, therefore, that primarily was devoted to the performance of function is now directed to growth, and there is then formed a mass of uncontrolled cells. This view gains support in that many of the malignant tumors appear at a time when the function of the tissue is at a decline.

A general survey of the field would indicate that true tumors are not parasitic in nature. That the condition is one in which the potential activity of the cell is sufficient to give rise to unlimited growth if the restricting barrier, whatever that may be, be removed. To that extent the cancer cell itself may be considered in the light of a parasite. It has been shown that in the rat certain tissues ordinarily resistant to the implantation of bits of rat tumor may become susceptible as a result of some

pre-existing irritation. To this condition has been applied the term *precancerous stage*. In the human being there are certain lesions of the mammary gland that although in themselves non-cancerous may later become so.

Predisposing Causes.—*Age.*—Certain tumors apparently bear a distinct relationship to the age of the individual. Before thirty years the sarcomata are most likely to appear; after that period, the carcinomata.

Sex.—On account of the frequent involvement of the female genitalia women are much more commonly the victims of cancer than men.

Heredity may have some influence, as it has been found that carcinomata are more common in some families than in others.

Occupation, as in chimney-sweepers and in paraffin-workers, who seem to frequently suffer from carcinoma. Probably the result of chronic irritation due to a lack of cleanliness.

Morphology.—Tumors may differ greatly in the following respects:

Size.—They may be of any size, from microscopic to weighing 275 pounds, as reported by Delameter.

Shape.—According to their shape tumors are called *nodular* when spheric, *tubercles* when projecting as a rounded body above the surface of an organ, *flat* or *tabular* when rising as a comparatively level elevation.

When the growth is connected to its original site by a stalk or pedicle it is called a *polyp*. When the surface is very roughened and irregular the tumor may be termed a *cauliflower* or *dendritic* growth.

If like a mushroom with a narrow stalk and a broad head, it is termed a *fungus*.

Color.—The color of a growth depends upon the nature of the tissue of which it is composed, upon the amount of blood present, and the presence of pigment. It may also be modified if degenerative processes have taken place.

Consistency depends upon the structure of the growth and upon the presence or absence of degenerations. If of bone the tumor will be very hard; if of mucous tissue, very soft.

Number.—Tumors may be *single* or *multiple*, there being usually a single *primary* tumor with several *secondary* ones if the growth is malignant, these latter being of the same type as the primary. There may, however, be hundreds of primary tumors, as in cases of fibroma molluscum. Sometimes there may be several primary tumors of different histologic types.

A *recurrent* tumor is one that recurs at the place from which it was removed.

According to the arrangement, tumors may be *typical*, *hemoplastic*, or *homologous* when they resemble the tissue from which they arise; *atypical*, *heteroplastic*, or *heterologous* when they differ.

If made up of a simple tissue they are called *histoid* tumors; if of a combination, attempting the formation of an organ, *organoid;* and when containing portions of all three blastodermic layers, *teratoid*.

The blood-vessels, which always originate from pre-existing vessels, may be greatly increased in number, *telangiectatic;* in size, *cavernous;* or unusually arranged, *plexiform*. These may be greatly decreased in number, thereby favoring secondary changes, or their walls may be imperfectly formed, giving rise to hemorrhages. Capillaries are commonly absent. Lymphatics are usually present, but the nervous supply is very poor, as a rule.

The *growth* of a tumor is independent of that of the individual. It may continue even if the normal tissues are being sacrificed for it. A lipoma will grow although the patient may not be getting sufficient nourishment to carry on the normal functions of the body.

It may be either *central expansion*, as is the case in benign growths, or *peripheral infiltration*, as in the malignant forms. The latter also increase by means of the central expansion.

As the blood-supply of tumors is usually poor, they frequently undergo various forms of degeneration, as *pigmentation*, *calcification*, *fatty*, *hyaline*, *colloid*, and *mucoid* metamorphoses; *necrosis* and *ulceration*.

According to their effect upon the individual a new growth may be either *benign* or *malignant*.

Benign growths do not affect the patient except as they may press upon vital structures or undergo degenerative processes.

They are usually circumscribed, encapsulated, do not give metastases, and do not recur after excision.

Malignant tumors are those that through their own influences tend to bring about the death of the individual. They are not circumscribed nor encapsulated, cause cachexia, probably toxic in origin, give metastasis, and recur after excision.

depraved state of nutrit

Metastasis refers to the extension of the primary growth by the transference of malignant cells to other parts of the body. In *carcinoma* this takes place, as a rule, by means of the lymphatics. As the original tumor increases in size its cells penetrate the surrounding tissues, and on account of the decreased resistance tend to grow along the lymphatic spaces. In this way distant growths may be directly connected with the primary focus by means of these strands. This is frequently spoken of as the *permeation* method. As the tumor extends, it is the neighboring lymph-nodes that first show secondary involvement. The extension continues until a chain of lymph-nodes is attacked. It is also very probable that extension by means of the blood may occur indirectly in carcinoma. The tumor cells may gain entrance to the thoracic duct and thus get into the circulation. They then usually lodge in the liver and give rise to new masses. Under other conditions, such as necrosis and ulceration, the cancer cells can enter directly into the blood.

In *sarcoma* extension takes place only by means of the blood, the walls of the vessels being very incomplete and easily allowing the entrance of tumor cells.

Death may be caused by tumors—

1. *Pressing* upon vital organs.
2. *Invading* vital organs and causing degeneration.
3. *Hemorrhage* resulting from ulceration and degeneration.
4. *Absorption* of poisonous products.
5. *Secondary infection.*
6. *Exhaustion* due to the tumor using up so much nutrition for its own benefit.

Classification of Tumors.—The simplest is as follows:

I. HISTOID.

Simple Connective-tissue Tumors

	Atypical	*Typical*
Embryonic type	Sarcoma.	Connective tissue.
Adult type	Fibroma {Hard, Soft}	Connective tissue.
	Lipoma.	Fatty tissue.
	Myxoma.	Mucous tissue.
	Chondroma.	Cartilage.
	Osteoma.	Bone.
	Glioma.	Neuroglia.

Specialized Connective-tissue Tumors

Myoma { Rhabdo-	Striated muscle.
Myoma { Leio-	Non-striated muscle.
Hemangioma	Blood-vessels.
Lymphangioma	Lymph-vessels.
Lymphadenoma	Lymphatic tissue.
Lymphoma	Lymphatic tissue.

Type of Endothelium

Endothelioma.

II. ORGANOID.—*Epithelial Tumors.*

Neuroma	Nerve tissue.
Squamous epithelioma	Squamous epithelium.
Hard papilloma	Squamous epithelium.
Soft papilloma	Columnar epithelium.
Cylindric epithelioma	Columnar epithelium.
Adenoma, Hypernephroma	Normal glandular type of cells.
Carcinoma	Atypical glandular cells.

III. TERATOID.—*Mixed Tumors.*

Dermoids.
Teratoma.
Cholesteatoma.

IV. CHORIO-EPITHELIOMA, SYNCYTIOMA MALIGNUM.—*Deciduoma Malignum.*

Combinations of tumors that have been derived from the same blastodermic layer frequently occur, as fibrosarcoma, fibromyoma, etc. One type, however, cannot be transformed into another.

The following classification of Adami's is recommended as being the most logical on account of its having been based upon a careful study of the histogenesis of the tissues.

Adami explains the classification as follows: "We thus find that the embryo comes to exhibit cell collections of two orders, which may be termed 'lining membranes' and (for lack of a more expressive word) 'pulps,' the 'lining membranes' being the persistent epiblastic, hypoblastic, mesothelial, and endothelial layers, the 'pulps' being the main mass of the neuroblast (of epiblastic origin), the notochord (of hypoblastic), and the mesenchyme (of mesoblastic). And now, following up the development of these different cell collections, we observe that the adult tissues derived from these two series exhibit well-marked differences, so that we can divide adult tissues into two great groups—the *lepidic* (from λεπις, λεπδος, a rind, skin, or membrane) and the *hylic* (ςλη, crude undifferentiated material).

"The characteristic of the lepidic tissues is that the specific cells which give them their main features are arranged either in layers or clusters *in direct apposition; they are not separated by lymph-spaces or by blood-vessels;* they possess, nevertheless, a supporting framework or stroma of hylic tissue in which run the nutrient vessels. Of the hylic tissues, the features are the opposite: *separating the cells there is a matrix of intracellular substance*, either homogeneous or fibrillated, while *lymph-spaces and blood capillaries tend to separate and run between the individual cells.*

"If in the lepidic tissues there is a stroma of hylic tissues, so here in the hylic there always enters lepidic tissue in the shape of the living endothelium of the blood- and lymph-vessels. In either case the elements of the other order occupy a subordinate position. While some pathologists, like O. Israel and Buxton, have already noticed this distinction, the histologists and embryologists have laid little stress upon it. The more we study tumors, the more we realize the importance of the distinction."

On this basis we obtain the following classification of normal tissues:

I. LEPIDIC, OR LINING MEMBRANE TISSUES

in which the blood-vessels do not penetrate the groups of specific cells and in which there is an absence of definite stroma between the individual cells, although such stroma, of mesenchymatous origin, may be present between the groups of cells.

1. Epiblastic:
   Epidermis. Epidermal appendages of the hair, nails, enamel of the teeth, etc. Epidermal glands. Epithelium of the mouth and salivary glands. Epithelium and glands of the nasal tract and associated spaces. Epidermal portion of the hypophysis cerebri. The lens of the eye. Epithelium of the membranous labyrinth of the ear, anus, and male urethra (except the prostatic portion).
2. Hypoblastic:
   Epithelium of the digestive tract and glands connected with it. Specific cells of the liver, pancreas, tonsils, thymus, and thyroid. Epithelium of the trachea, lungs, bladder, female urethra, and male urethra (prostatic portion).
3. Mesothelial:
   Lining cells of the pleuræ, pericardium, peritoneum. Specific cells of the suprarenals, kidneys, testes, and ovaries (Graafian follicles). Epithelium and glands of the Fallopian tubes, uterus, vagina, vasa deferentia, vesiculæ seminales, etc.
4. Endothelial:
   Lining endothelium of the blood-vessels and lymphatics.

II. HYLIC, OR PRIMITIVE PULP TISSUES

Organs and tissues in which the special characteristic is that the specific cells lie in, and are separated by, a definite stroma, homogeneous or fibrillar, in which there may or may not be blood and lymph-vessels.

1. Epiblastic:
   Nerve-cells; neuroglia.
2. Hypoblastic:
   Notochord.
3. Mesenchymatous:
   Fibrous connective tissues, cartilage, bone, reticulum of lymph-glands, bone-marrow, fat-cells, involuntary muscle tissue, spleen, blood-vessels, blood-corpuscles.
4. Mesothelial:
   Striated muscle, including cardiac muscle.

"Following this scheme of classification of the normal tissues, we may now divide the tumors arising from the specific constituent cells of the various tissues into two main genera—the *lepidic* tumors or *lepidomata*, originating from the above 'lining membrane' tissues, and the *hylic* tumors (*hylomata*), originating from tissues derived from the embryonic 'pulp.' We can further distinguish two broad groups of lepidic tumors—the *primary*, those whose cells are derived in direct descent from

the original epiblast and hypoblast, and the secondary, or transitional, whose cells are derived in indirect descent from the same—*i. e.*, have in the course of development passed through a mesoblastic or mesenchymatous stage before coming to form portions of a lining membrane."

In the classification that follows the author has not followed the exact wording of Dr. Adami, but has introduced such modifications as shall be consistent with his own text:

I. LEPIDIC, OR RIND TUMORS

A. Lepidomata of the First Order

1. *Of Epiblastic Origin.*
   Tumors (epitheliomata) whose characteristic constituents are overgrowths of tissues derived directly from the epiblastic "lining membranes" or epiderm.
   (*a*) *Typical.*—Papilloma.
   Adenoma of the sweat-glands.
   Adenoma of the sebaceous glands.
   Adenoma of the mammary glands, etc.
   (*b*) *Atypical.*—Squamous-cell carcinoma.
   Carcinoma of glands of epiblastic origin.
2. *Of Hypoblastic Origin.*
   (*a*) *Typical.*—Papilloma of the digestive and respiratory organs and bladder.
   Adenoma of the digestive and respiratory tracts, thyroid, pancreas, liver, bladder, etc.
   (*b*) *Atypical.*—Carcinoma developing in the same organs and regions.

B. Lepidomata of the Second Order or Transitional Lepidomata

3. *Of Mesothelial Origin.*
   Tumors (mesotheliomata) whose characteristic constituents are cells derived in direct descent from the persistent mesothelium of the embryo.
   (*a*) *Typical.*—Adenoma of the kidney, testicle, ovary, urogenital ducts; uterus, prostate.
   Mesothelioma—adenoma of the serous membranes of the pleura, peritoneum, etc.
   (*b*) *Atypical.*—Cancer of the above-mentioned organs; squamous endothelioma, so-called, of serous surfaces, epithelioma of the vagina; adrenal mesotheliomata, hypernephroma.
4. *Of Endothelial Origin.*
   Tumors (endotheliomata) originating from the endothelium of the blood- and lymph-vessels:
   Lymphangio-endothelioma.
   Hemangio-endothelioma.
   Perithelioma.
   Cylindroma.
   Psammoma.
   Cholesteatoma.

II. HYLIC, OR "PULP" TUMORS

1. *Of Epiblastic Origin.*
   Tumors whose characteristic constituents are overgrowths of tissues derived from the embryonic pulp of epiblastic origin.
   (*a*) *Typical.*—Neuroma.
   Glioma.
   (*b*) *Atypical.*—Gliosarcoma.
2. *Of Hypoblastic Origin.*
   Tumors derived similarly from embryonic pulp of hypoblastic origin.
   Chordoma.
3. *Of Mesenchymal Origin.*
   A. *Mesenchymal Hylomata.*—Derived from tissues originating from the persistent mesoblastic pulp or mesenchyme.
   (*a*) *Typical.*—Fibroma.
   Lipoma.
   Chondroma.
   Osteoma.
   Myxoma.
   Leiomyoma.
   Angioma.
   Myaloma.
   Lymphoma.
   (*b*) *Atypical.*—Derived from mesenchymatous tissues.
   Sarcoma.—Fibrosarcoma.
   Spindle-cell sarcoma.
   Oat-cell-shaped sarcoma.
   Chondrosarcoma.
   Osteosarcoma.
   Myxosarcoma.
   Lymphosarcoma.
   Chloroma.
   Angiosarcoma.
   Melanosarcoma (debatable).
   B. *Mesothelial Hylomata.*—Tumors which are overgrowths similarly of tissues derived from embryonal pulp of definitely mesothelial origin.
   Rhabdomyoma.

TUMORS OF EMBRYONAL CONNECTIVE TISSUE

SARCOMA

A *sarcoma* is a tumor made up of cells that resemble physically those found in embryonal connective tissues. As a rule the greater the departure from the adult cell, the greater is the malignancy. They are characterized by the preponderance of the cells over the intercellular substance, which may be granular, fibrillary, or reticular. The sarcoma cells are not truly embryonal, as they never continue to a complete development.

They arise from the mesoblastic layer and often retain the characteristics of the tissue from which they arise, periosteal sarcomata sometimes containing bone.

The sarcomata are essentially malignant; that is, they infiltrate the surrounding tissues, give metastases, cause cachexia, and return after excision. It is only occasionally that they are encapsulated.

The blood-vessels are generally few in number and imperfectly formed, the single layer of endothelium being supported by a very few connective-tissue fibers. In many cases the

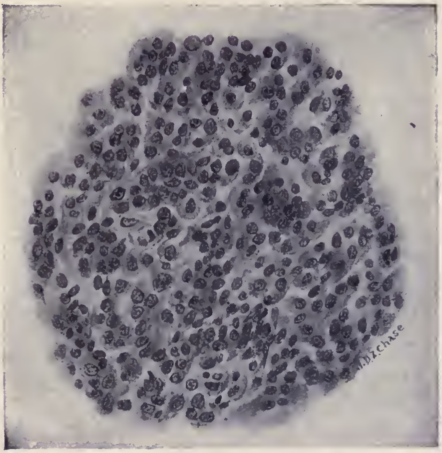

FIG. 39.—SMALL ROUND-CELL SARCOMA OF THE LOWER JAW. Oc. 3; ob. D. D. (McFarland).

blood-channels are simply spaces whose walls are formed by the tumor cells. The imperfect vessel wall explains why hemorrhage in these tumors is so common and why *metastasis* takes place by means of the blood.

Sometimes the blood-spaces may be very large and numerous, thus forming the angiosarcoma.

As a rule, no lymphatics are present.

Sarcomata may occur in any part of the body; as a rule, they are seldom primary within organs.

They generally occur before the age of thirty. Are frequently rounded in shape, somewhat lobulated, and to a certain degree circumscribed. Are hard or soft according to the amount of intercellular substance present, or to the variety of the tissue of which they are composed.

Their color is generally pink or grayish; this, however, depends to a great extent upon the condition and number of the blood-vessels.

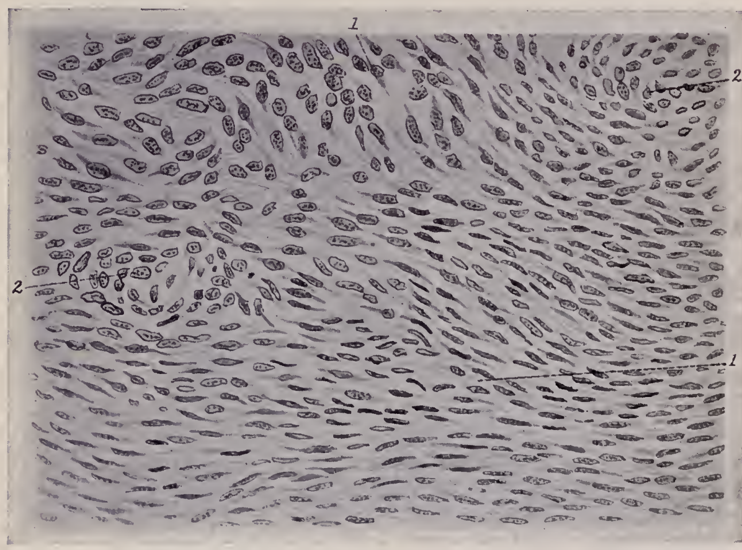

FIG. 40.—SPINDLE-CELL SARCOMA FROM THE BRAIN. × 300 (Dürck). 1, Spindle cells cut longitudinally; 2, spindle cells in transverse section.

mucous tumor

On account of the poor blood supply, degenerations, particularly *myxomatous*, frequently take place. Interstitial hemorrhages as a result of the degeneration are not infrequent.

If there is pigment present, either melanin or hemosiderin, the tumor is called a *pigmented* one.

These tumors vary greatly in their malignancy, the small round-cell type, especially if melanotic, being rapidly fatal. The greater the amount of cellular elements, the greater is the malignancy.

The **varieties** of the tumors depend upon the kind of cell that predominates.

1 *Round-cell sarcomata* are those made up of either *large* or *small* round cells.

In the *small*-cell variety the intercellular substance is very scanty. They are rather soft, whitish in color, friable, and a milky juice can be scraped from the cut surface.

FIG. 41.—GIANT-CELL SARCOMA OF THE THIGH (McFarland).
a, Giant cells; *b*, spindle cells.

They grow rapidly, infiltrate the surrounding tissues, give extensive metastasis, recur quickly after removal, and soon cause death. They may occur in any part of the body and at any age.

The individual cells have large vesicular nuclei, that stain deeply, and comparatively little protoplasm.

If there is a close resemblance to the arrangement of a lymph-

node, small round cells with a distinct reticulum, the tumor is called a *lymphosarcoma*.

The *large round-cell sarcoma* is very similar to the small, but is firmer on account of the intercellular connective tissue present. The cells are larger, and although generally round, may be polygonal, and are sometimes arranged in alveoli.

Are less malignant than the small.

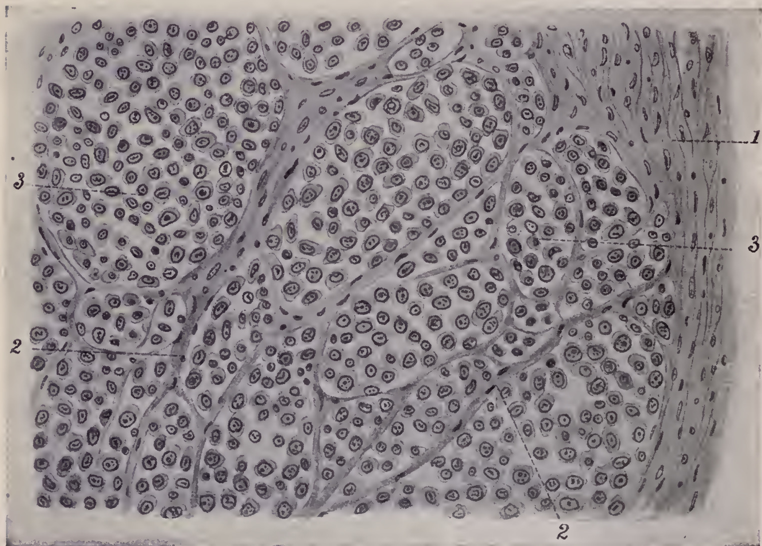

FIG. 42.—ALVEOLAR LARGE ROUND-CELLED SARCOMA FROM THE PERIOSTEUM. × 250 (Dürck).

1, Heavy septum of connective tissue; 2, delicate connective-tissue reticulum; 3, polyhedral cells with vesicular nuclei.

2 *Spindle-cell sarcoma* is one that is made up of spindle cells, either large or small. Is one of the commonest forms.

These tumors are quite firm, white, and very little juice can be scraped from the cut surface. The cells are arranged in irregular bundles and have oval vesicular nuclei. The amount of intercellular tissue may be very great, making the tumor quite hard; is then known as a *fibrosarcoma* and is but slightly

malignant. It is often difficult to determine whether the tumor is a sarcoma or a fibroma.

The spindle-cell sarcomata are relatively benign; they frequently do not give metastasis, although recurring after removal.

3 *Giant-cell sarcoma* is one in which there are found cells made up of a large amount of cytoplasm in which are numerous oval nuclei centrally located. The predominating cells may be round or spindle shaped. They are most commonly found in

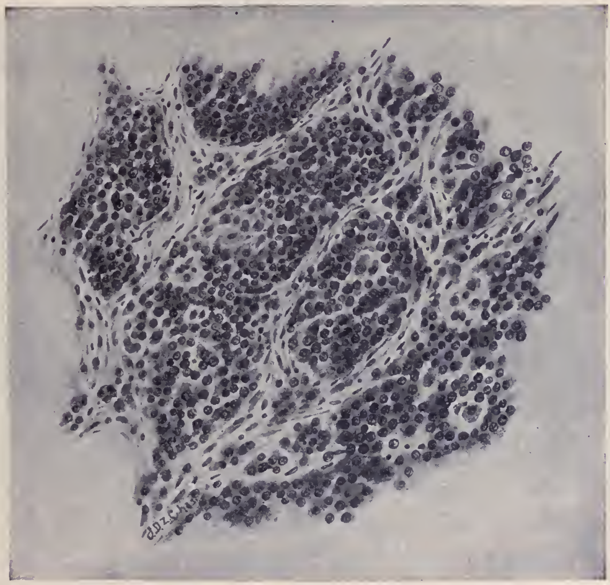

FIG. 43.—ALVEOLAR SMALL ROUND-CELL SARCOMA. Zeiss, Oc. 4; ob. c. (McFarland).

relation with bone and periosteum. When occurring on the jaw are sometimes referred to as *epulis*, although the same term may be applied to a simple fibrous tumor.

This form is the least malignant of all the sarcomata.

Special names have been given to other forms of sarcoma on account of some special feature.

4 *Alveolar sarcoma* is where either groups of round or spindle

cells are surrounded by distinct bands of connective tissue. This form may very closely resemble carcinoma.

5 *Melanotic sarcoma* is one of any type in which there is *melanin* present. This pigment may be found either in the cells or in the intercellular tissue.

They occur in the skin, the choroid coat of the eye, and in the ciliary body.

Are very malignant, give widespread metastasis, and rapidly

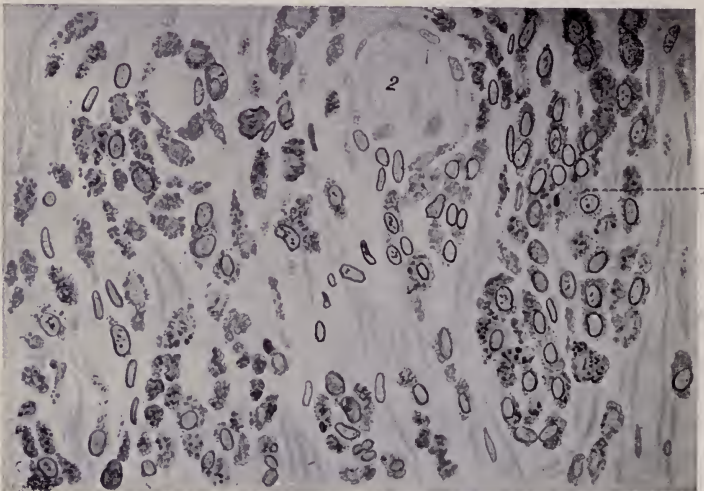

FIG. 44.—METASTATIC MELANOSARCOMA OF THE PERITONEUM. × 320 (Dürck).

1, Nests of darkly pigmented polygonal cells; 2, cross-section of vessels.

prove fatal. The liver is the common secondary seat, particularly after primary melanotic sarcoma of the eye.

6 *Myxosarcoma* is one in which there is a marked mucoid degeneration present.

7 *Angiosarcoma* is a growth that contains many blood-vessels. If the walls of these vessels or the neighboring cells undergo a hyaline degeneration, the sarcoma is spoken of as a *cylindroma*.

If the tissue with the exception of those cells in the imme-

diate neighborhood of the vessels undergoes a mucoid change, the growth is called a *myxangiosarcoma tubulare*.

8 *Chloroma* is a variety of sarcoma arising from the periosteum of the skull; is greenish in color. It may be that this form is more closely related to the tumor formations occurring in leukemia.

FIG. 45.—PERITHELIOMA OF THE RETINA (McFarland). *a*, Blood-vessels surrounded by cells in a good state of preservation; *b*, degenerated portion of tumor.

9 *Psammoma* is a tumor allied to the sarcoma. It is made up of masses of spindle cells, which contain areas of hyaline degeneration and calcification. Are usually found in the meninges of the brain and spinal cord.

10 *Endothelioma* is a tumor arising from endothelial cells. These growths are at times very difficult to differentiate from carcinoma

on account of the apparent cell nest arrangement, but careful examination will commonly show some sarcomatous areas.

The cells extend along the lymphatic spaces and are closely related to connective tissue. Are found in the serous membranes, testicle, ovary, liver, and parotid. Are malignant.

Under this same heading are included those tumors develop-

Fig. 46.—Endothelioma of the Pleura. Zeiss, Oc. 2; ob. c. (McFarland).

The illustration shows the cellular growth in the form of cylindric masses which fill crevices of the tissue, probably originally channels.

ing from the cells in the lymph-spaces, the *lymphangio-endothelioma;* and those from the endothelium of the blood-vessels, the *hemangio-endothelioma.* Occasionally some of these tumors arise from the perivascular endothelium, and to these has been given the name *perithelioma.* The cells in these latter are arranged in strands radiating from the vessel around which the mass originated.

According to the combination of tissues present sarcomata may be further classified as follows: all such varieties, however, not being mentioned:

Osteosarcoma	=	bone present.
Chondrosarcoma	=	cartilage present.
Myosarcoma	=	muscle present.
Neurosarcoma	=	nerves present.

TUMORS OF ADULT CONNECTIVE TISSUE

Fibroma is a tumor of fibrous connective tissue. Fibromata are usually pale in color, round, lobulated, circumscribed, and encapsulated. They may be of varying degrees of firmness.

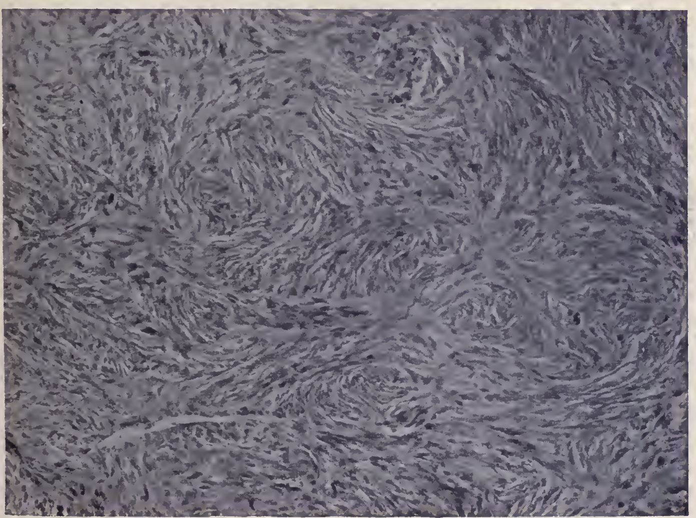

FIG. 47.—FIBROMA. CELLS AND FIBRILS IN SMALL BUNDLES WHICH RUN IN EVERY DIRECTION (Mallory).

The cells resemble those of normal connective tissue and are arranged in bundles that cross each other in all directions.

In the *soft* variety the cells are separated by serous or mucous deposits.

In the *hard* variety the cells are closely packed together.

Fibromata are benign and frequently undergo various degenerations. Occur in all parts of the body, particularly in the uterus, where they attain great size. In this locality are usually combined with muscle tissue, forming the *fibromyomata*.

They may occur in combination with sarcoma, or any of the various forms of adult connective tissue, as fibrolipoma, myxoma, chondroma, etc.

A *keloid* is a fibrous tumor that forms usually from a scar. It is not confined to the seat of the original injury, but extends somewhat into the surrounding tissues. Is usually smooth, and is most frequently seen in negroes.

Molluscum fibrosum is a condition in which there is a non-inflammatory overgrowth of the fibrous structures of the nerves, particularly those of the skin and subcutaneous tissues. Such tumors may occur singly or be present by the thousand over all parts of the body.

Epulis is a fibrous growth originating from the gum, usually at the site of diseased teeth.

Myxoma is a benign tumor made up of mucous tissue. Is usually pale in color, round, lobulated, encapsulated, and feels semifluid. On section a thick, viscid fluid exudes.

Microscopically spindle and stellate cells with long processes that anastomose are seen. In the meshes between the cells and processes is the mucous material. This substance is precipitated by acetic acid.

They occur in sheaths of tendons and nerves and in nasal and pharyngeal polyps, and in combination with sarcoma. Mucoid growths forming from degeneration of fibromata are not true examples of myxomata.

Lipoma is a benign tumor made up of fatty tissue. Is yellow in color, round, lobulated, encapsulated, and soft. May be very large. Microscopically the cells resemble ordinary fatty tissue, except in being considerably larger and the connective-tissue trabeculæ are also thicker than normal. Occurs most commonly in the subcutaneous tissue, in fasciæ, and in synovial membranes. Is slow in growth and will frequently persist even if the individual is much emaciated. The blood-supply

is poor, and such tumors may undergo various forms of infiltration and degeneration, as calcification ossification, necrosis, etc.

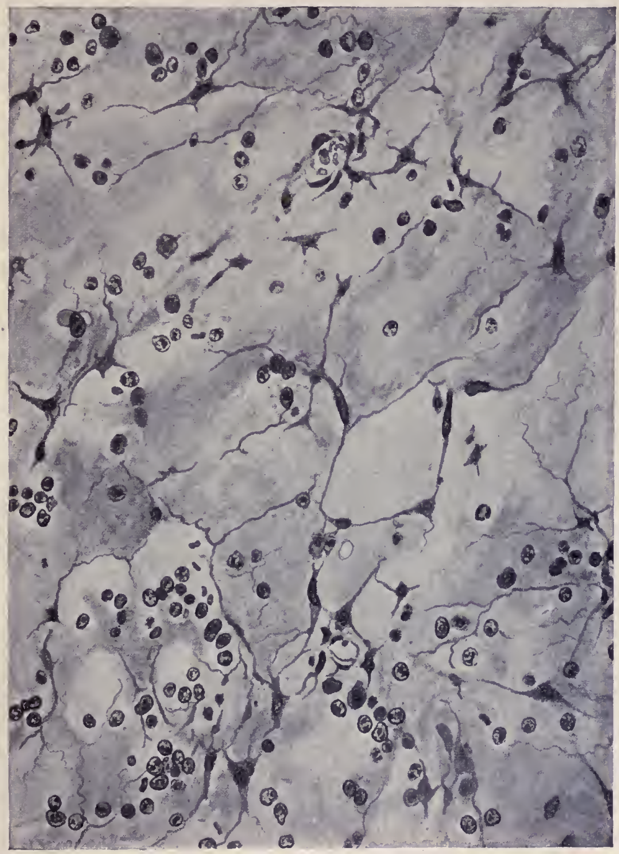

Fig. 48.—Myxomatous Fibroma of the Nasal Mucous Membrane (Dürck).

Stellate connective-tissue cells joined together with protoplasmic processes; the intercellular substance has become myxomatous and contains abundant masses of leukocytes.

Occurs in combination with sarcoma, myxoma, fibroma, and angioma.

Chondroma is a growth composed of either hyaline or fibrous cartilage.

Arises from pre-existing cartilages, periosteum, or the medullary substance of the long bones. If it is found in localities where periosteum does not exist, as in the testicles and lungs, is called an *enchondroma.*

Is hard, encapsulated, and lobulated. Is slow in growth, may persist for years, and become very large.

Frequently undergoes mucoid degeneration and calcareous infiltration.

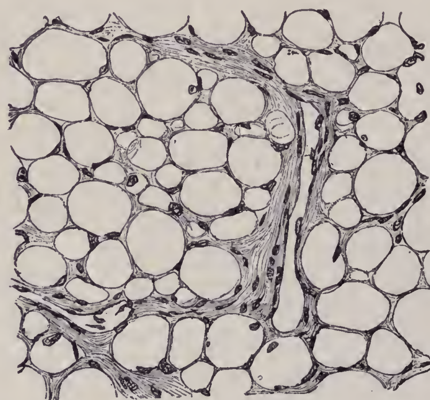

Fig. 49.—Lipoma from the Region of the Shoulder with Relatively Small Fat Cells. (M. Fl. Häm.) × 300 (Ziegler).

Is benign, but in combination with sarcoma may be quite malignant. Is also found in combination with lipoma, fibroma, and myxoma. An *ecchondroma* is a small overgrowth of cartilage. Are found on the edges of the articular, laryngeal, and nasal cartilages.

Osteoma is a tumor composed of bone. It may be a result of inflammatory processes of the periosteum or be a distinct new growth.

If developing from a bone-forming tissue, is called an *homologous* osteoma.

If arising in a tissue that is not bone forming, is called a

heterologous osteoma. The latter are found in the meninges, lung, and parotid gland.

An osteoma is a hard, bony, rounded, and more or less lobulated growth. Microscopically it presents quite typically the normal structure of bone. May be composed of spongy or compact new bone, osteoma spongiosum and osteoma durum.

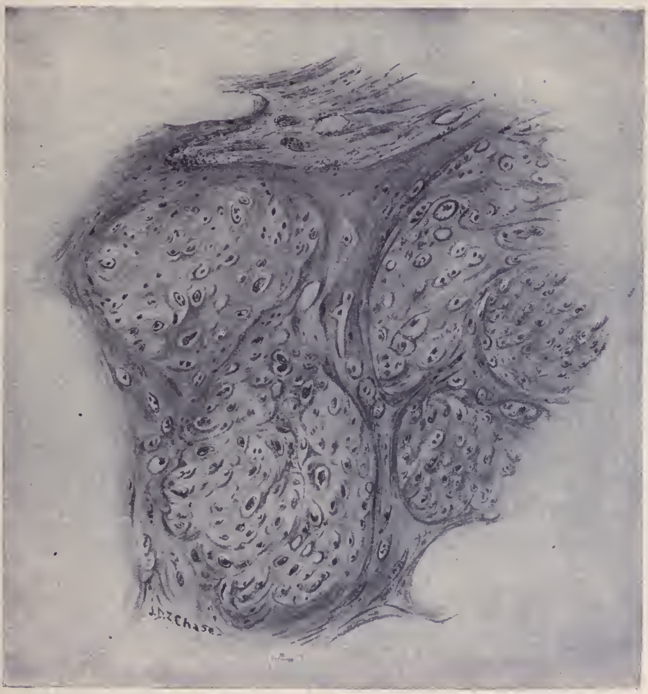

FIG. 50.—HYALINE CHONDROMA. Oc. 2; ob. 3 (McFarland).

If the growth is small, circumscribed and flat, and arising from pre-existing bone, it is called an *osteophyte*. If irregular and projecting, an *exostosis*.

Occurs most commonly at the epiphyses of long bones. Is benign. May be in combination with cartilage, fibrous tissue, fat, or sarcoma, in which latter case it is malignant.

Myoma is a tumor composed of newly formed muscle-fibers. According as to whether the muscle is striped and voluntary, or unstriped and involuntary, we have the *rhabdomyoma* and the *leiomyoma.*

The first is very uncommon, but occurs in the kidney, heart, and uterus.

The latter occur frequently in the uterus and broad ligament, but may arise wherever there is involuntary muscle.

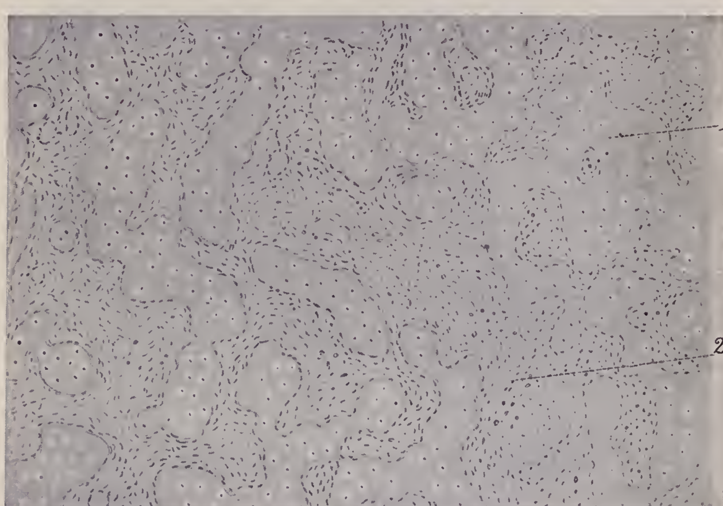

FIG. 51.—OSTEOMA OF THE LUNG. × 75 (Dürck).
1, Bone-trabeculæ; 2, fibrous interspaces not presenting the characters of medullary spaces.

May be single or multiple. Are firm, round, lobulated growths, dark reddish in color. Microscopically they consist of elongated spindle cells, with rod-shaped nuclei collected in bundles that interlace in all directions.

Are benign, slow of growth, and frequently undergo cystic or calcareous degeneration. The cysts contain mucus.

Usually are in combination with fibroma.

Neuroma is a tumor composed of nerve tissue. As the

term has been applied to all growths found on nerves, two divisions are made; the *true* neuroma, which consists of nerve tissue; and the *false* neuroma, which consists of fibroconnective tissue.

FIG. 52.—LEIOMYOMA OF THE UTERUS (Uterine, Fibroid). Oc. 4; ob. 3. (McFarland).

The true is called a *ganglionic* neuroma when ganglionic nerve-cells are present; if nerve-fibers only are present, it is called a *fibrillar* neuroma.

Hemangioma is a tumor made up of blood-vessels separated by a small amount of connective tissue.

Angioma simplex or *nevus* when the vessels are small and

very much interwoven. To this class belong the reddish discolorations known as birth-marks.

Cavernous angioma when the blood-spaces are large and separated by distinct fibrous bands. Resembles the structure of the corpus cavernosum of the penis.

Plexiform angioma when a group of more or less parallel blood-vessels become tortuous and widely dilated.

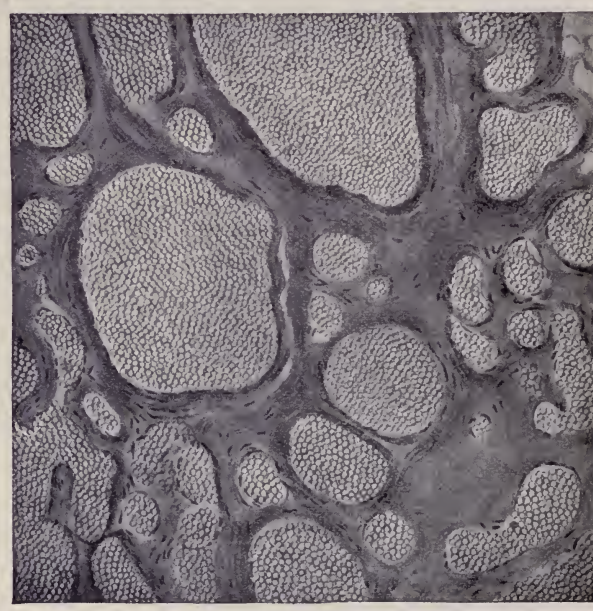

FIG. 53.—CAVERNOUS ANGIOMA (Warren).

Lymphangioma is a tumor caused by a dilatation of lymphatic vessels with an arrangement quite similar to that of the hemangioma.

An **odontoma,** according to Bland-Sutton, from whose work the following is taken, is a tumor composed of dental tissues in varying proportions and different degrees of development, arising from the teeth germs, or teeth still in the process of growth.

The species of this genus are determined according to the part of the tooth germ concerned in their formation.

1. Epithelial odontoma	= from the enamel organ.
2. Follicular odontoma, 3. Fibrous odontoma, 4. Cementoma, 5. Compound follicular odontoma,	= from the tooth follicle.
6. Radicular odontoma	= from the papilla.
7. Composite odontoma	= from the whole germ.

1. *Epithelial odontoma* occur, as a rule, in the mandible, but they have been observed in the maxilla. They have a fairly

FIG. 54.—EPITHELIAL ODONTOMA. NATURAL SIZE (Bland-Sutton).

firm capsule, and in section display a collection of cysts of various shapes and sizes, but the openings rarely exceed 2 cm. in diameter. The cysts are separated by thin fibrous septa, sometimes ossified. The cavities contain a brown mucoid fluid which gives a reddish tint to the growing portions of the tumor. Histologically, an epithelial odontoma consists of branching and anastomosing columns of epithelium, portions of which form alveoli. The cells occupying the alveoli vary, the outer layer may be columnar, while the central cells degenerate and give rise to tissue resembling the stellate reticulum of an enamel organ. It may be that many of these tumors do not arise from the epithelial enamel organ, but from endothelium within the gums.

2. *Follicular odontoma* comprise those swellings often called

"dentigerous cysts," an inaccurate term. They arise commonly in connection with teeth of the permanent set, and especially with the molars. Sometimes they attain large dimensions and produce great deformities, particularly when they arise in the upper jaws and happen to be bilateral. Occasionally they occur in connection with supernumerary teeth. The tumor consists of a wall of varying thickness, which represents an expanded tooth follicle; in some cases it is thin and crepitant, in others it may be as much as 1 cm. thick. The cavity of the cyst usually contains viscid fluid and the crown or the roof of an imperfectly developed tooth. Occasionally the tooth is loose in the follicle, sometimes inverted, and often its root is truncated. Exceptionally the tooth is absent, or is represented by an ill-shaped denticle. The walls of the cyst always contain lime or osseous matter, the amount varying considerably. These tumors are not unknown in other animals, having been found in sheep, pigs, and porcupines. The amount of fluid in a follicular odontoma varies, and the size of the tumor depends in the main upon this. Sometimes the fluid may measure as much as 2 ounces, and this may lead to the wide separation of the inner and outer plates of the body of the mandible, and the odontoma may occupy the entire length of the bone.

3. *Fibrous Odontoma.*—In a developing tooth, a portion of the connective tissue in which it is embedded is found to be denser and more vascular than the rest; it also presents a fibrillar arrangement. This condensed tissue is known as the tooth sac, and, when fully developed, presents an outer firm wall and an inner looser layer of tissue. At the root of the tooth the follicle wall blends with the dentin papilla, and is indistinguishable from it. Before the tooth cuts the gum it is completely enclosed within this capsule. Under certain conditions this capsule becomes greatly increased in thickness and so thoroughly encysts the tooth that it is never erupted. Such thickened capsules are mistaken for fibrous tumors, especially if the tooth be small and ill developed. Under the microscope they present a laminated appearance, with strata of calcareous matter. To these the term "fibrous odontomata" may be

applied. As a rule they are multiple, four being by no means an unusual number. There is good reason to believe that rickets is responsible for some of these thickened capsules.

4. *Cementoma.*—When the capsule of a tooth becomes enlarged, and these thick capsules ossify, the tooth will become embedded in a mass of cementum. To this form of odontoma the name "cementoma" may be applied. Tumors of this character occur most frequently in horses. The chief structural peculiarity is the presence, in enormous numbers, of large, richly branched openings.

5. *Compound Follicular Odontoma.*—If the thickened capsule ossifies sporadically instead of uniformly, a curious condition is brought about, for the tumor will then contain a number of small fragments of cementum, or dentin, or even ill-shaped teeth (denticles) composed of three dental elements—cementum, dentin, and enamel. The number of teeth or denticles varies greatly, and may reach a total of four hundred.

6. *Radicular odontoma* is the term applied to those tumors which arise after the crown of the tooth has been completed, and while the roots are in the process of formation. As the crown of the tooth, when once formed, is unalterable, it naturally follows that should the root develop an odontoma, enamel cannot enter its composition; the tumor would consist of dentin and cementum in varying proportions, these two tissues being the result of the activity of the papilla. The outer layer of the odontoma is composed of cementum; within this is a layer of dentin, and inside this is a nucleus of calcified pulp. It is probable that some radicular odontomata in man are due to inflammatory changes.

7. *Composite odontoma* is a convenient term to apply to those hard tooth tumors which bear little or no resemblance in shape to teeth, but occur in the jaws, and consist of a disordered conglomeration of enamel, dentin, and cementum. Such odontoma may be considered as arising from an abnormal growth of all the elements of a tooth germ, enamel organ, papilla, and follicle. Not only is this growth composite in that the tumor originates from all the elements of a tooth germ, but it is composite in another sense: many of these tumors are composed

of two or more tooth germs indiscriminately fused. But they differ from the cementomata containing two or more teeth in the fact that the various parts of the teeth composing the mass are indistinguishably mixed, whereas the individual teeth implicated in a cementoma can be clearly defined. It was long believed that composite odontomata occurred only in the mandible, but it is clear not only that they arise as frequently in the maxillæ, but that they attain a far larger size in the upper than in the lower jaw.

Dental Cysts.—It occasionally happens that in extracting permanent teeth a small fibrous bag is found at the apex of the root, often no larger than an apple seed, though sometimes it may be as large as a bantam's egg, filled with fluid, and often containing crystals of cholesterin. These sacs, or dental cysts, occur in connection with the dead roots of mandibular and maxillary teeth, especially molars and premolars. They sometimes attain a considerable size in the upper jaw when they invade the antrum, and some of these cysts are sufficiently large to simulate an abscess of that cavity. Dental cysts are often bilateral and occasionally multiple. The constant association of these cysts with the dead roots of permanent teeth has led many observers to regard them as pus-sacs with thick fibrous walls. Others, having demonstrated the existence of an epithelial lining in many of these cysts, believe that they arise in embryonal "rests," known as "paradental epithelial remnants."

TUMORS OF EPITHELIAL TISSUES

A **papilloma** is a benign tumor composed of projections of fibrous connective tissue that are covered by one or more layers of epithelium, either squamous or columnar in type.

May be divided into the *hard* and the *soft* papilloma.

The *hard* occur on the skin as warts, and when so situated are commonly pigmented; also around the genitalia as a result of constant irritation, in which situation they are known as "venereal warts." Are also found on the true vocal cords in the larynx. Are covered by squamous epithelium which commonly undergoes keratosis, a horny change. In this form the

"pearly bodies" or "epithelial pearls" are frequently found. These are made up of cells concentrically arranged, many of which have lost their nuclei and have become transformed into keratin. They are found only in squamous epithelium.

Papillomas covered by squamous epithelium are frequently found in the urinary bladder, and, although histologically benign, they very frequently undergo malignant changes.

FIG. 55.—TUFT OF PAPILLOMA OF THE BLADDER (Stengel).

The *soft* papillomas occur in the intestine, and are covered by columnar epithelium. This form quite frequently undergoes malignant transformation.

The connective-tissue stalks may be simple projections or very complicated, branching outgrowths. They contain blood-vessels and lymphatics.

An **adenoma** is a tumor that in its structure resembles an

FIG. 56.—PAPILLARY ADENOMA FROM THE RECTUM. Hemat.-eosin. × 98 (Dürck).

1, Vascular stroma; 2, stratified cylindric epithelium.

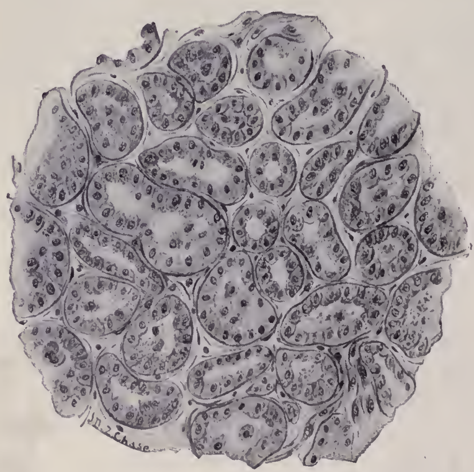

FIG. 57.—ALVEOLAR ADENOMA OF THE MAMMARY GLAND. Oc. 2; ob. 9 (McFarland).

epithelial gland. It is frequently very difficult to tell whether it is a true growth or only an enlargement of a normal gland.

In the new growth the tissues, though arranged typically, do not carry on any useful function. The secretion may be imperfect or there may be no duct through which it can escape.

Adenomas arise from epithelial glands, are circumscribed, encapsulated and rounded, or nodular. Have been found in all glandular tissues.

FIG. 58.—FIBRO-ADENOMA OF THE MAMMARY GLAND (CANALICULAR FORM). Oc. 2; ob. 3 (McFarland).

Microscopically they consist of a framework of connective tissue, the meshes of which are covered by one or two layers of epithelial cells that resemble in shape and size those of the normal glands. The important point that distinguishes these growths from malignant ones is the relation of the cells to the basement membrane. In the benign adenoma the membrane

is preserved and the cells show no tendency to invade the surrounding tissue.

If the connective tissue and epithelium are in normal proportion the growth is called a *simple adenoma;* if the connective tissue predominates, a *fibro-adenoma.*

If the tumor has a pedicle, it is known as an *adenomatous* polyp.

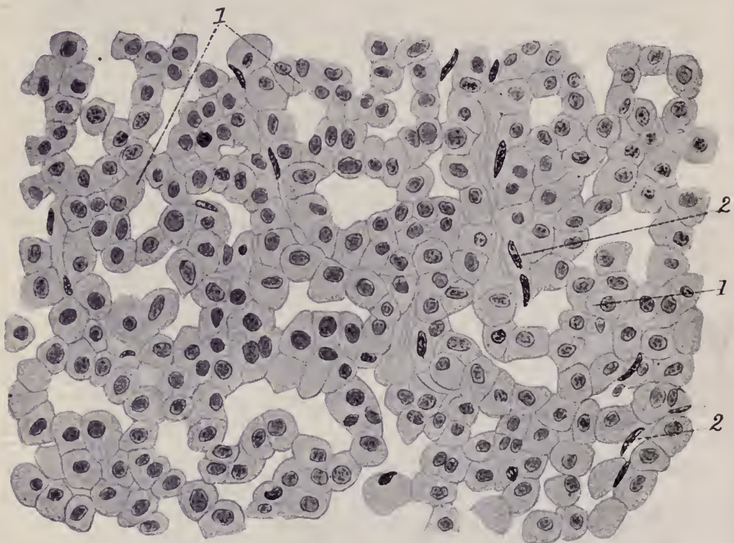

Fig. 59.—Adrenal Tumor from the Kidney (Hypernephroma) (Dürck).

1, Large polygonal cells, containing an abundance of fat and arranged in tubes; 2, connective-tissue cells in the scanty stroma.

Through degenerations, particularly colloid or mucoid, an adenoma may become very large through cystic formation. It is then called an *adenocystoma.*

If villi extend into the acini in the above form the growth is called an *adenocystoma papilliferum.*

Hypernephroma are tumors that resemble the cortical portion of the adrenal gland. They probably arise from misplaced portions of adrenal tissue, and, as such "rests" consist

of only cortical elements, these tumors do not resemble the medulla of the gland nor do they contain epinephrin. Are found most commonly in the upper pole of the kidney, liver, broad ligament, and in other abdominal tissues.

Although commonly benign and encapsulated, they may take on a malignant change, infiltrate, and give rise to metastases by means of the blood-vessels.

The cells are large and vesicular, with large round, centrally placed nuclei. The connective-tissue framework is very slight. Dilated capillaries and areas of hemorrhage are common.

Gliomas are growths composed of neuroglia or nervous connective tissue. As they arise from the epiblast, they cannot be classified with the mesoblastic tumors.

Are usually small, reddish in color, and not distinctly limited from surrounding tissues.

Microscopically they are composed of cells with large nuclei and with long fine processes.

Blood-vessels may be numerous and many areas of hemorrhage present.

Are benign and slow growing.

CARCINOMA

A **carcinoma** is a malignant tumor of epithelial origin. It is characterized by a marked proliferation of epithelium with infiltration into the surrounding tissues.

The epithelium is arranged atypically in a supporting framework made up of adult connective tissue.

The epithelial cells are not characteristic of the growth, but they differ in some respects from the normal type. The diagnosis of carcinoma cannot be made from the cell, as there is no distinct cancer cell. The general arrangement of epithelium and connective tissue must be taken into consideration.

The carcinomatous epithelium frequently consists of cells many times larger than normal. Their nuclei may be unusually large, vesicular, and show a peculiar affinity for nuclear stains, a condition called *hyperchromatosis.*

*

They may divide by an atypical mitosis and give rise to peculiar arrangements of the chromatin. These cells multiply rapidly, and, though at first round, they may become almost any shape on account of the mutual pressure exerted. In some cases giant cells occur. Tumors of this variety differ greatly in size, shape, color, and density.

Carcinomas are composed of two types of tissue, epithelial

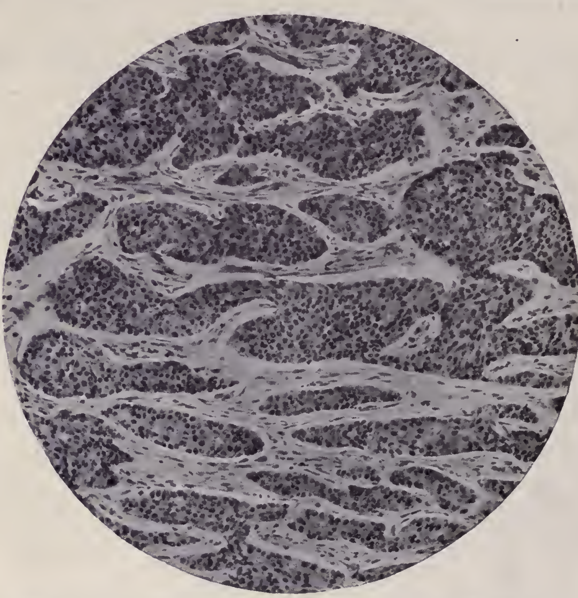

FIG. 60.—CARCINOMA OF MAMMARY GLAND (Mallory). Medullary type of growth. Slight tendency to the formation of gland lumina.

and connective, cells and stroma. According to the one that predominates, carcinoma are called *medullary* when the cells are more numerous; *scirrhus* when the tumor is rich in connective tissue.

The first is soft; the second, hard.

Well-developed blood-vessels and lymphatics are found in the stroma, which is most likely derived chiefly from pre-

existing connective tissue, but a certain amount is probably newly formed. Elastic fibers are present in the infiltrating portion of the growth, but they are fragments of fibers preexisting in the invaded tissue. The cellular elements originate from the epithelium normal to the part involved, and frequently retain the characteristics of the primary cell.

The more closely connected it is with the original cell, the

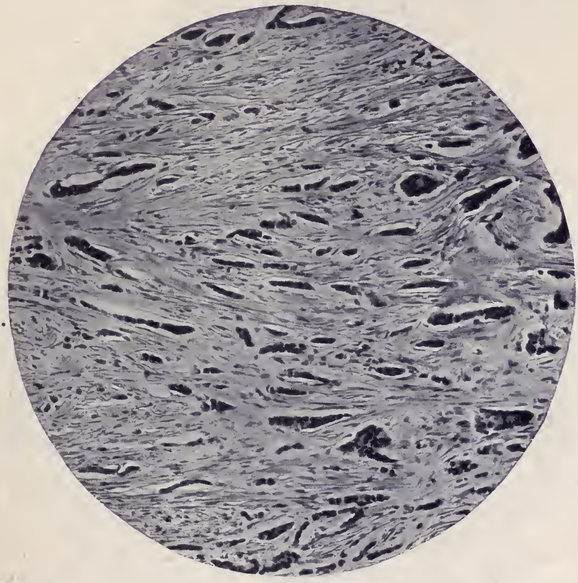

Fig. 61.—Scirrhous Carcinoma of Breast (Mallory). Alveoli of epithelial cells small; stroma abundant.

more does the carcinoma cell resemble it. The further away it is, the greater is the variation. There is then a tendency to revert to the round, undifferentiated, embryonal type. Between the cells no fibrillary substance is found.

In carcinoma the cells frequently undergo degeneration, and usually of a form peculiar to the parent tissue. If it arose from squamous epithelium, keratin is found; colloid or mucoid material if derived from mucous membranes. The

tumor may break down and undergo a fatty change, most common in the mammary gland.

A carcinoma may become infected and show marked inflammatory changes which may be so great as to somewhat disguise the true character of the growth. There will be an infiltration of the tissues with leukocytes.

Microscopically a carcinoma consists of columns of cells running in all directions, separated from one another by fibrous tissues. These columns give the appearance of alveoli filled

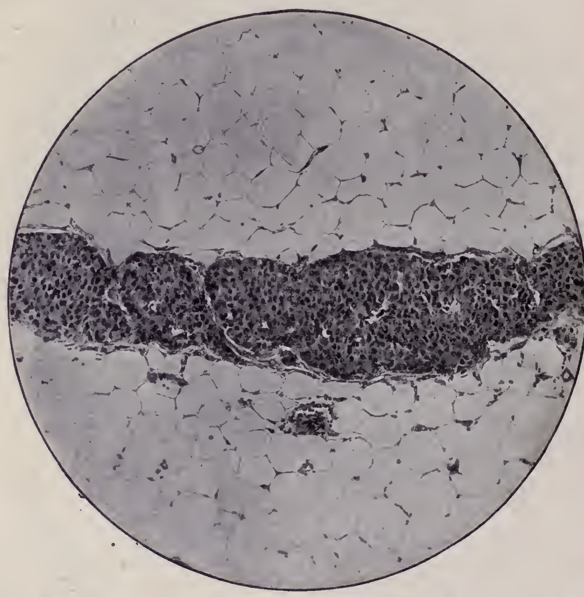

Fig. 62.—Carcinoma of Mammary Gland (Mallory and Wolbach). Extension of tumor through a lymphatic in fat tissue.

with epithelium. The columns are branched into numerous subdivisions, giving a complicated root-like structure.

As the tumor grows these cells infiltrate and ramify in all directions, occupying usually the lymphatic spaces. Along the advancing border there is a more or less well-marked zone of round-cell infiltration.

As there is no intracellular substance, the cells easily break away from the main mass and are carried to the neighboring lymph-nodes. This may take place very early and give rise to extensive metastasis. These secondary growths are usually similar in character to the primary.

Extension to distant tissues may be due to *permeation.*

FIG. 63.—SQUAMOUS EPITHELIOMA (McFarland).
a, Epithelial masses; *b*, epithelial pearls; *c*, connective tissue; *d*, capillary blood-vessels.

According to this theory there is a continuous growth of cancer cells along the lymphatics of the deeper fascia, with widespread involvement.

A **squamous epithelioma** is a carcinoma that has arisen from a surface covered by stratified epithelium such as skin and certain mucous membranes. It occurs most commonly on

the cervix, the skin of the face, penis, vagina, and esophagus, especially wherever there is a junction of skin and mucous surfaces.

It makes its appearance as an indurated mass in which ulceration takes place rapidly and exposes a circular surface with raised, hard edges. Sometimes it looks at first like a small wart.

Columns of these cells penetrate the tissues and on account of pressure arrange themselves in successive layers, the inner ones being almost flat and cornified, forming the *epithelial pearls*. *Hyperkeratosis* is the term used to indicate the cornification.

The presence of these pearls does not indicate that the tumor is necessarily malignant; they mean that the growth was derived from squamous epithelium. They are also not always found in squamous epitheliomata. The growth may have been so rapid as not to have allowed cornification to take place. As the cells infiltrate the surrounding tissue, there is a well-marked border zone of round cell infiltration, and the elastic tissue, as a rule, shows various forms of degeneration.

The cells are usually quite large, and may show numerous "prickles."

This form of carcinoma differs greatly in its malignancy. Some may exist for several years without showing much tendency to spread, but may suddenly grow and cause extensive destruction of tissue, with subsequent death of the patient. They recur on removal, and give metastasis by the lymphatics.

X-ray Carcinoma.—As a result of long-continued exposure to the *x*-ray, chronic dermatitis very commonly develops. The superficial cells become necrotic, but in addition there is an involvement of deeper structures. Necrotic foci occur in the corum, probably due to vesicular disturbances, such as narrowing of the lumen of the vessels due to a proliferation of the endothelium. These deeper lesions may remain quiescent, but eventually the epidermis undergoes a downward proliferation, invades these foci, takes on an infiltrating character, and may give rise to very extensive metastases. The fingers and hands are usually the site of the primary lesion or lesions. The

histologic structure of these growths is that of the squamous epithelioma.

Rodent ulcer or *carcinoma basocellulare* arises from the basal cells of the epidermis, particularly from those cells in the hair-follicles. Are most common in the region of the eyes and nose, usually occurring in men.

For many years—from three to twelve or more—there may

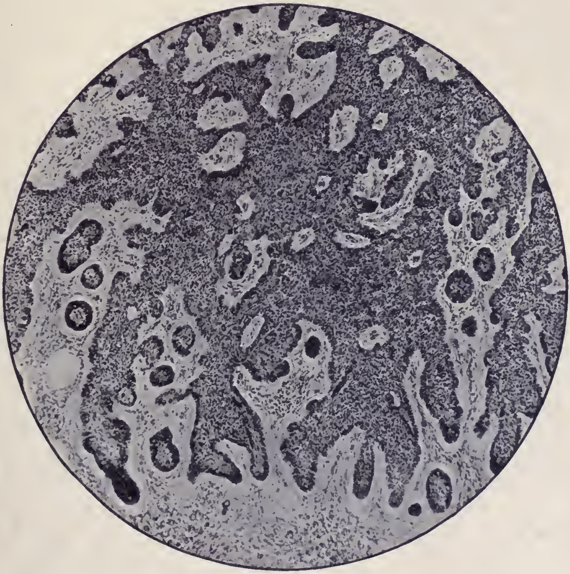

Fig. 64.—Rodent Ulcer (Mallory).

be present a smooth, rounded nodule, the size of a pea. This may then break down and form an ulcer with rounded, smooth, and firm pearly gray edges. The ulceration may extend widely, bringing about extreme destruction of all the invaded tissues. It very rarely undergoes cicatrization, and seldom if ever gives metastasis or involves lymph-nodes. The cell nests have a peculiar roset form, due to the short, blunt projections of cells at the periphery. The nuclei are, as a rule,

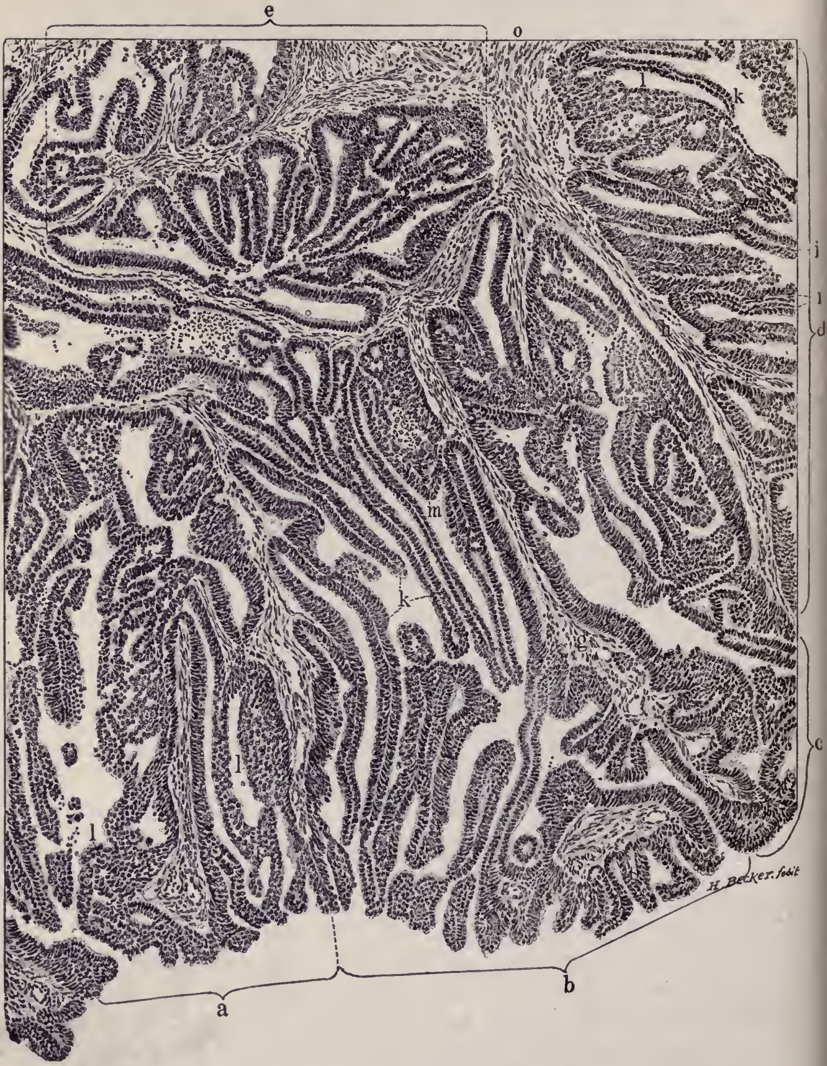

FIG. 65.—ADENOCARCINOMA OF THE BODY OF THE UTERUS (Cullen).

o, May be likened to a main stem from which arise numerous secondary stems, which in turn give off delicate terminals, consisting entirely of epi-

long, narrow and spindle shaped, and do not stain deeply. At the periphery of the cell nests the nuclei are arranged somewhat radially.

It is usually single, but may be multiple and may continue for many years—three to twenty-four.

An **adenocarcinoma** is a cancer in which the glandular structure is to a great extent preserved, but the epithelium has taken on a proliferative growth. It either breaks through the basement membrane or else fills up the acini with numerous layers of cells. It is commonly found in the stomach, intestines, and uterus. Grows rapidly, gives metastasis, and quickly proves fatal.

The development of carcinoma differs greatly in different people. In some cases a continued mild irritation may precede. The growth may be very slow, but if for some reason there is an increase in the nutrition, as in the pregnant uterus, it may suddenly become rapid.

If the growth is rapid and metastasis extensive, the health of the patient suffers and cachexia develops. This may be the result of pain, of suppurative conditions, or from the absorption of toxic substances resulting from the disturbance of metabolism.

The etiology of carcinoma is still obscure. Heredity is apparently clear in many cases as a predisposing cause.

Age is of importance, the majority of cases appearing after thirty-five, a time when the resisting power of the tissues is beginning to diminish.

Carcinoma is more common in women than in men. In women it is in the genital organs; in men, in the intestinal tract.

Irritation and injury seem to at least be of some importance as exciting causes, although in themselves it is doubtful if they can give rise to a carcinoma.

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thelial cells. The glands may be divided into groups *a*, *b*, *c*, *d*, and *e*, by the stems of stroma *f*, *g*, and *h*. The stems are covered by several layers of cylindric epithelium, while projecting into the gland cavities are long slender ingrowths of epithelium, devoid of stroma, as seen in *i*. Very delicate ingrowths consisting merely of two layers of epithelium are seen at *k* and *k*. At *l* the epithelium is several layers in thickness, and at *m* many layers with leukocytes. The arborescent character of the growth and peculiar gland grouping are characteristic of adenocarcinoma.

Loss of resistance of the connective-tissue stroma has been advanced, but does not seem logical. Many observers have tried to prove that these growths are infectious processes, the results of parasitic activity. Many cellular inclusions resembling protozoa have been found, but the general opinion at present is that these bodies are nothing more than degenerated cells or secretions of cells. Experiments to prove the infectious nature of carcinomata have not been generally successful. The transplantation of cancer tissue into a normal

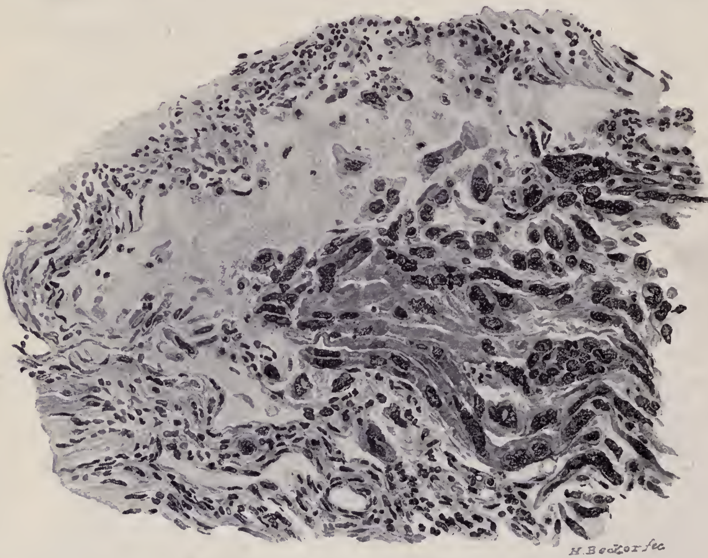


FIG. 66.—SYNCYTIAL MASSES INVADING A VENOUS CHANNEL IN A CASE OF DECIDUOMA MALIGNUM (J. Whitridge Williams).

individual has failed. But when placed in another situation in the person from whom the tissue was excised growth has followed. This has frequently been considered proof of the parasitic nature. It probably means nothing more than that the pieces of tissue have found surroundings favoring their growth; a condition such as occurs in skin-grafting.

Bacteria, protozoa, sporozoa, gregarinæ, blastomycetes,

amebæ, and fungi have all been suggested as the cause. These claims, however, rest upon the form of the bodies and their staining properties, not upon cultivation and inoculation. Until these latter can be carried out the parasite theory must remain unproved.

CHORIO-EPITHELIOMA

The following discussion and classification is taken from Adami and McCrae:

To properly understand the formation of the chorio-epithelioma it will be necessary to review briefly the origin of the fetal placenta. This structure, arising from chorionic villi, finally develops a vascular mesoblastic core covered by epiblast. The outer cells of the fetal chorion erode into the mucous membranes of the uterus. Normally these cells, when they have penetrated into the sinuses, have done their work, and the outer layer becomes inactive, fuses, and forms the syncytium. Sometimes in cases of abortion these placental changes, usually complete by the time of full term, have not yet occurred, and when the immature fetus is expelled, there remain chorionic cells which have not degenerated and are still actively growing. These constitute the evil agent; they continue their growth in the uterus and form a neoplasm.

Placental Mole.—In some instances the fetus may die, be absorbed, and leave the placenta and membranes grafted upon the uterus in the form of an irregular fleshy mass, prone to hemorrhage and to putrefaction. On the other hand, the chorionic villi, being nourished by maternal blood, may grow actively and absorb fluid so that a villus becomes a vesicle or a series of vesicles. These may be large or small, due to distention by an edematous mucoid fluid. These vesicles may eventually take up as much room as a full-term fetus. Such an edematous mass of vesicles is known as a *hydatid mole.*

Chorio-epithelioma.—Such a hydatid mole as above described may pass beyond the usual growth and fill the uterine sinuses with polypoid masses, the so-called destructive placental polyp. The outer surface of the villus, consisting of

fetal epiderm, becomes fused to form syncytium, which is made of deeply staining cells whose bodies have fused, the mass thus being multinuclear. Below the syncytial layer the cells of Langhans' layer remain unfused, individual, and less deeply staining. The syncytium possesses erosive and phagocytic properties, and it is these masses of cells that tend to be swept away in the blood of the maternal sinuses and to be deposited in the capillaries of the lung and elsewhere.

Chorio-epithelioma Malignum.—This term is applied to a neoplasm that is entirely cellular, formed of large actively vegetative cells growing entirely within the vessels, not requiring an individual blood-supply by vessels of its own, not capsulated, liable to induce hemorrhage by erosion of the vessel walls, and very readily tending to have particles carried away to grow elsewhere. Such a tumor generally occurs shortly after an interrupted pregnancy, but may not occur for years after an abortion with no intervening pregnancy. Microscopically, various cells are seen. Very large ones containing many large nuclei, rich in chromatin, are formed by direct division. Others, much smaller, with single well-formed nuclei. Some that resemble lymphocytes, and all kinds of forms resembling the above types more or less closely. In places there may be found long narrow strands of protoplasm containing nuclei, but showing no division into individual cells, syncytium. Clinically, these tumors show great variations in malignancy, although microscopically their structure may be similar.

TERATOMA

Under this heading are included those tumors which have a tendency to the formation not only of irregular cell masses, but also of fully formed organs, such as brain, teeth, skin, hair, bone, or secreting glands. Such growths may be due to the development of two germinal areas on one germinal vesicle, giving rise to double monsters, one of which undergoes inclusion in the other—*fetal inclusion*. They may result from the displacement of totipotential cells—those capable of giving origin to an individual—which become included in the growing

organism. These cells may develop early and grow elaborately, giving rise to inclusions recognizable at birth. They may lie latent and at a subsequent time grow actively as abdominal inclusions, teratoma of the genital glands, and certain mixed tumors.

Dermoid cysts, ovarian dermoids are the most common of the teratoma. The cyst cavity is lined by squamous epi-

FIG. 67.—TEETH FROM OVARIAN DERMOID (From Coplin after Roberts).
An irregular branching piece of bone contained in a dermoid cyst of the ovary, in which are implanted well-formed teeth: 1, 1, Bony mass; 2, a tooth resembling a canine of the first dentition; 3, 3, 3, teeth resembling molars.

thelium in which are found sweat and sebaceous glands. Within the cavity is usually a varying amount of fatty material in which are masses of hair. In the wall of the cyst are found masses of bone to which teeth, usually but poorly formed, are

attached. In some instances the extremities and genitalia have been seen.

Somewhat similar growths may be found in those parts of the body where fetal clefts have united and in the median fissures of the body.

There is another type, the **sporadic teratoma,** which grow in regions bearing no relationship to the fissures, to the poles of the body, or to the generative glands, as in the anterior mediastinum and the abdomen. These are probably due to the development of a misplaced totipotential cell. They generally consist of tissues from all three germinal layers. Sometimes the tissues are of adult appearance and of limited growth. More frequently they appear about puberty, grow rapidly, and tend to form secondary tumors.

CYSTS

A *cyst* is a collection of a fluid or semifluid substance contained within a connective-tissue wall lined by epithelium or endothelium. The contained material may be serous, mucous, or purulent if infection has occurred.

Cysts may be either single or multilocular. The latter when divided into numerous compartments by fibrous partitions. These division walls may break down and convert a multilocular into a simple cyst.

Cysts may be divided into the following:

1. *Retention* cysts, resulting from an obstruction to the outflow of the secretion of a gland.

2. *Exudation* cysts, those formed by an increase of fluid in a closed cavity, as in the tunica vaginalis.

3. *Necrotic* or *liquefaction* cysts result from the breaking down of the central portion of solid tumors.

4. *Parasitic* cysts may occur on account of an inflammatory reaction around the parasite, or may be formed directly by it in its development.

5. *Dermoid* cysts belong to the teratomata, where they are described.

6. *Cystoma*, a cyst of neoplastic formation. They most frequently occur in the ovary and are multilocular.

CHAPTER XI

INFECTION

By **infection** is meant the successful invasion of the tissues by an organism. The mere presence of the living agent within the body is not sufficient to cause infection; it must enter the tissues and give rise to symptoms that indicate a diseased condition. Trypanosomes may be even within the blood-vessels of certain animals and cause no symptoms.

There are normally many organisms contained within the body, particularly in the alimentary canal, but they give rise to no pathologic conditions until they leave their accustomed habitat.

Infection, therefore, means the entrance of organisms into the body, with subsequent injury to the tissues involved. By an infective disease is meant one that is the result of the entrance into and the multiplication of the organisms within the body.

The symptoms in such a condition are the results of the formation of toxins, and not of mechanical disturbances. As a rule, no symptoms appear immediately after the entrance of the invading organism into the body, as there is not sufficient toxin present. The interval between the inoculation and the symptoms resulting from the toxins is known as the *period of incubation*, which differs greatly in different diseases.

Then, too, infection may be influenced by certain peculiarities of the infecting organism and of the attacked individual. It is a well-recognized fact that true infection does not always occur after the primary invasion. This may be due to variations in the ability of the micro-organism to produce disease. Some have very little power to multiply after gaining entrance into the tissues, but they may form large amounts of poison. Other bacteria may form but little poison, yet have almost

unlimited powers of multiplication when in the body. The number of the organisms and the mode of entrance also effect the severity of the infection.

The infecting organisms may come from outside of the body—*exogenous*. They may enter the lungs in consequence of impure air or they may gain entrance into the body along with the food or water. Wounds of various sorts may carry the organisms into tissues; then, too, it has been discovered that diseases may be conveyed from one person to another by biting insects.

Endogenous infections are those resulting from organisms that are commonly present within the body. They may be due to some change in the tissues of the host, that allow these living bodies to escape from their normal surroundings and gain entrance into unusual localities. The colon bacillus that is normal in the intestinal canal may cause much trouble if it gets into other localities. It must be remembered that practically all openings communicating directly or indirectly with the external air will contain bacteria. They are normally present in the skin and the adjacent mucous membranes. The mouth and the intestines contain many varieties, while the stomach, on account of its acid contents, contains but few. The normal lungs are free from bacteria.

The results of bacterial invasion are much influenced by the local conditions at the point of attack—the avenue of infection. These are of the greatest importance in determining the occurrence or non-occurrence of infection. Certain bacteria, such as those of cholera, typhoid, and dysentery, attack only the intestinal canal, and will not cause trouble unless they first gain access to that tract. The gonococcus will not produce an infection in skin, even if that tissue be wounded. The tubercle bacillus in the lung can cause widespread destruction; in the skin little appears other than a localized tubercle.

Of the various obstacles to infection, an intact epithelial covering of the body inside and out is probably the most important. Such a covering is an efficient barrier against staphylococci and streptococci. An injury, nevertheless, need be but very slight in order to permit the organisms to enter. Such an injury may be secondary to the destructive action of prod-

ucts formed by the bacteria themselves. Associated infections may, likewise, be of importance. Tetanus organisms may not survive if inoculated alone into normal tissues, but will grow if pyogenic bacteria are also present. The same probably holds good with the diphtheria bacillus. Both of these, although unable to grow and multiply in an intact structure, can do so when these tissues have been previously or simultaneously bruised or lacerated. Although the epithelial coverings can protect, yet injuries to them are very common, and bacteria frequently gain entrance to the tissues. The question then arises, Why does not every infection become generalized and lead to the destruction of the host? There are two factors concerned in this problem. One is the *aggressive* or attacking force of the micro-organism, the other is the resistance which the host offers to the presence of the invader, to its multiplication, or to its ability to produce harmful substances. This resisting power is the *defensive* force.

Aggressive Forces.—Certain bacteria, as those of diphtheria and tetanus, are possessed of a very low grade of infectiousness, by which is meant their power of multiplying in the invaded body. The infection is almost always strictly local during the life of the individual; a general infection being exceedingly rare, and occurring as a terminal or a post-mortem condition. The tetanus bacillus, particularly, is practically unable to maintain itself in normal living tissues. In cases of infection it owes its limited development either to the damage done by an associated infecting agent or by direct mechanical injury. Even then the organism has frequently disappeared from the body entirely at the time when the patient is actually dying from the effects of its brief sojourn. Evidently, its aggressive powers are minimal and, even though it kills through its highly poisonous toxin, the resistance which the animal body offers to its presence is entirely sufficient to prevent its active development. Similar conditions exist in regard to the diphtheria bacillus. It is questionable whether it can gain access to the deeper tissues through intact superficial structures, but by means of its own toxin it is evidently capable of causing marked destruction after that superficial barrier has

been passed. The above instances show that the infectious and toxic properties of an organism are two independent factors, which in the case of tetanus and diphtheria bear an inverse relation to each other.

An altogether different behavior is seen in a group of organisms represented by the anthrax bacillus and that of chicken-cholera. In these the local infection is followed almost immediately by a generalized infection, the organisms not only living, but actually multiplying freely in the body of the host. Their aggressivity, as compared with the previously mentioned type, is greatly developed, while their toxicity is practically nothing.

Between these two types already mentioned stand the cholera vibrio and the typhoid bacillus. Their aggressivity is quite well developed, particularly that of the typhoid bacillus, which is commonly present in the blood and tissues. In addition to their aggressiveness, the organisms of this class possess a well-marked toxicity, the effect of this appearing quite early in the course of the infection, and leading to a fairly characteristic clinical picture of the corresponding infectious disease.

Generally speaking, it may be said that the ability of micro-organisms to do harm depends upon the injurious nature of the substances they can produce. There are probably three groups of substances that are now recognized as of importance in connection with the clinical picture of the infectious diseases. They are:

1. True toxins or exotoxins, extracellular and soluble.
2. Endotoxins, intracellular and insoluble.
3. Bacterial proteins.

Toxins.—According to Ehrlich, the following are the characteristics of toxins:

1. They are extremely easily destroyed (labile) substances which occur as secretion products of vegetable or of animal organisms.

2. Their chemical nature is unknown. The impossibility of obtaining them in a pure form and their great lability render them insusceptible to ordinary chemical analysis.

3. An analysis of a toxin may be reached at present only through the medium of animal experiment.

4. The introduction of toxins into the tissues causes the formation of an antitoxin with the production of immunity. It has not been possible to obtain antitoxins for inorganic poisons, as the alkaloids.

5. In contradistinction to well-defined chemical poisons, the action of toxins is characterized by a latent or incubation period. The incubation period may be shortened experimentally by the injection of large quantities of toxin, but it cannot be eliminated entirely. Snake-venom, however, seems to act without an incubation period, but it is still to be classed with toxins because of its power to cause the formation of antitoxin.

6. The facts make it necessary to assume as a condition for the poisonous action of toxins a specific union with the protoplasm of the cells in certain organs. The affinity of other poisons, as alkaloids, for tissues depends not upon specific chemical union, but on some such process as solid solution or loose salt formation.

The true toxins cause the physiologic and pathologic disturbances as a result of their solubility and the ease with which they can diffuse throughout the animal juices. The two chief toxin producers are the organisms of tetanus and diphtheria. A few of the tetanus bacilli may cause no local disturbance, yet may bring about the death of the individual. Toxins produce specific symptoms; consequently, it may be assumed that they have special selective affinities for certain tissues, and produce their symptoms in consequence of such affinity. This can be shown experimentally: a mixture of guinea-pig brain and tetanus toxin will prove harmless, although there may be present several times the fatal dose of the toxin. Other toxins, instead of being specific for the motor nerve-cells, may act upon the red blood-cells, or upon the leukocytes, or upon the cells of the respiratory centers, for instance.

Endotoxins are insoluble substances not secreted by the living organism, but set free only after the death and disintegration of the parasites. They are not as specific in their action as the true toxins, but their injection into suitable animals gives

rise to the production of antitoxins which are capable of neutralizing the endotoxin employed. The toxic effect rapidly diminishes on keeping, and is seriously impaired by exposure to higher temperatures—55° to 60° C. Many symptoms of disease may be due to the breaking down of the organism with the liberation of these bodies.

Bacterial proteins constitute the main mass of the organism. They differ from the toxins and endotoxins in not conforming to the characteristics of either of the two. Their effect is essentially pyogenic, the formation of pus, and is one common to most, if not all, bacteria. In some animals the pyogenic action does not manifest itself, because death results too early, but in more resistant individuals it can be shown. These proteins in themselves are not markedly dangerous, but they have gained in importance since it has been demonstrated that the introduction of foreign albumins leads not to increased resistance (immunity) against such proteins, but to hypersensitiveness (anaphylaxis). Consequently, a subsequent injection after a certain interval of time may produce serious symptoms or death.

Ptomains are nitrogenous compounds of basic nature and alkaloid-like properties, formed from animal matter in consequence of bacterial decomposition. Their formation is only possible when special food stuffs are directly available, while toxin production is, within certain limits, independent of the food supply, and represents a specific function on the part of the micro-organisms in question.

THE CARDINAL CONDITIONS OF INFECTION

Infection can take place only when the micro-organisms are sufficiently virulent, when they enter in sufficient number, when they enter by appropriate avenues, and when the host is susceptible to their action.

Virulence refers to the disease-producing power of micro-organisms which depends upon the invasiveness of the bacteria, the toxicity of their products, or both. This property may vary greatly in different strains of the same variety of

organism. Most bacteria when grown in artificial media will not be as virulent as those grown in some animal. If, however, animal fluids are added to the culture-media the virulence may be retained or even increased. In order to increase the virulence, the best results can be obtained by the transplantation of the organism from one animal to another without any intermediate growth on culture-media. This method, however, increases the virulence of the organism only for that particular kind of animal used. Transference through rabbits increases the virulence for rabbits, but not for other kinds of animals. This increase can continue to a certain point, beyond which it will not go. The number of organisms which is necessary to kill the animal becomes progressively smaller, and the period of incubation, the time between infection and the first symptoms, shorter, until finally a strain is obtained in which the degree of virulence can no longer be increased by animal passage. This constitutes the "virus fixe."

Number.—The number of bacteria gaining entrance has a very important bearing upon infection, and may determine whether it shall occur or not. When bacteria gain entrance into an animal there will always be some of the organisms that are unable to withstand the defensive powers of the host, and consequently perish. Others may be so weakened as to be unable to cause trouble, while some will be able to overcome the resistance, and give rise to disease. The more virulent the organism, the fewer will be the number required to infect.

Avenue of Infection.—Local conditions are of the greatest importance in determining the occurrence or non-occurrence of infection. Cholera, typhoid, and dysentery attack the digestive tract alone. The gonococcus apparently can invade only through the mucous membranes of the genito-urinary apparatus or of the eye. The tubercle bacillus, although able to invade any tissue of the body, gives rise to modified forms of the disease. If it invades the skin a local condition known as *lupus* occurs. This may last for years without becoming general. The same organism entering the lungs can give rise to consumption, with extreme destruction of tissue and generalized

infections. Skin infections in general tend to remain localized unless the organisms have been implanted quite deeply, so as to more readily gain access to the circulation.

The chief obstacle to infection no doubt lies in the integrity of the epithelial coverings of the body, both inside and out. An injury, however, need be but very slight in order to allow the micro-organism to gain entrance.

Susceptibility of the Host.—This varies greatly, some animals readily succumbing to infection by a certain organism, while other animals will be distinctly resistant. This resistance, however, may depend very largely upon the physical condition of the invaded individual. If anything occurs that will lower the general physiologic activity, the individual will then be less able to withstand the attack of the organisms. *Fatigue* is an apparent factor. When tired out, from one cause or another, infection is much more likely to occur. *Exposure*, particularly to cold, is a very common cause of lowering the bodily resistance, and thus allowing infection. *Diet* appears to have some obscure effect in predisposing to certain diseased conditions. *Intoxication* by poisonous substances increases the susceptibility to infection. This is quite commonly seen in the frequency and fatality of pneumonia among excessive indulgers in alcohol. *Injuries* of all sorts render the possibility of infection to become greater.

When two different types of organisms invade the body at the same time the resulting condition is known as a *mixed infection.*

If after one organism has caused tissue changes, another gains entrance and gives rise to pathologic conditions, it is called a *secondary infection.*

IMMUNITY

By **immunity** is meant the power to resist invasion by micro-organisms with the subsequent development of disease. An individual may be exposed to infection, but on account of some ability present may be able to resist and not acquire the disease.

The lack of resisting power is known as *susceptibility.*

One form of immunity is the *natural*, in which there is an inherited resisting power that is common to certain races of men or of lower living beings. The second type is the *acquired*, in which the immunity has been obtained after birth, and may be either active or passive.

Immunity is termed *active* when it results from the action of the cells within the invaded body, either in destroying the bacteria or in neutralizing their injurious products. It is that form which follows an attack of an infectious disease and which lasts for a varying period. It may be very brief, as in cholera; for a longer time, as in typhoid; or sometimes for life, as in small-pox. It may be due to accidental infection; to the inoculation of a weakened virus, as in vaccination; to the introduction into the body of bacterial products without the microorganism; or it may result from the inoculation of dead bacteria, as in bacterination.

Passive immunity is always acquired, never natural. It is that which is obtained by the introduction of the serum of an immunized animal into the body of a non-immune individual. The serum should always be introduced parenterally, that is, into the blood, subcutaneous tissues, or endothelial cavities, never by mouth, as it would then be acted upon by the digestive juices. It is supposed that in the serum of the first there is a substance that neutralizes the bacterial products in the blood of the infected animal.

It must be remembered that immunity is a comparatively relative term. An animal may resist an ordinary dose, yet succumb if a very large amount, either of bacteria or toxin, be administered. The degree of immunity may be reduced by unhygienic surroundings, by fatigue, by exposure to abnormal temperatures, abnormalities of diet, drugs, pre-existing disease, and by injuries.

Theories of Acquired Immunity.—1. Pasteur and Klebs believed that the bacteria growing in the body used up some material that was necessary for their growth, and after dying left an unsuitable soil. This theory is not borne out by the facts.

2. Wernich and Chaveau held that in the growth of bacteria

there were elaborated substances that inhibited their future development or activity. This theory also does not hold.

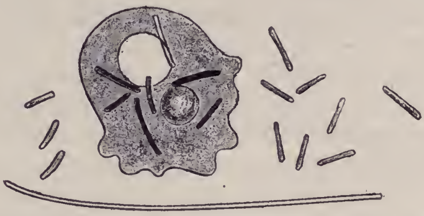


FIG. 68.—LEUKOCYTE WITH INCORPORATED BACILLI, ILLUSTRATINS PHAGOCYTOSIS (Metchnikoff).

3. The theory of phagocytosis. This is one of the most important, and is strongly supported by many well-known investigators. It, however, does not seem to be as satisfactory

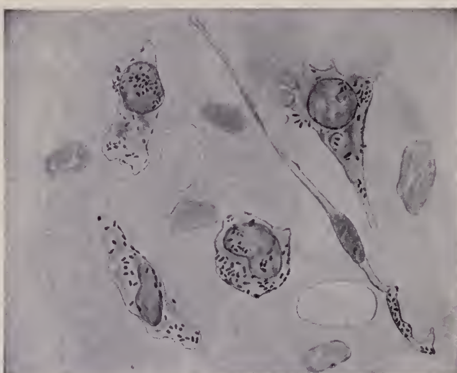


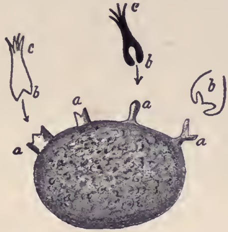
FIG. 69.—PHAGOCYTOSIS: THE OMENTUM IMMEDIATELY AFTER INJECTION OF TYPHOID BACILLI INTO A RABBIT.

Meshwork showing a macrophage, intermediate forms and a trailer, all containing intact bacilli (Buxton and Torrey).

in general application as Ehrlich's "side-chain theory," which will be discussed later.

There are certain cells in the body that have the power of ameboid motion, by means of which they are able to surround and take up bacteria and destroy them. These cells are known

as phagocytes. Metchnikoff believes that immunity is the result of the positive and negative chemotaxis (power of at-



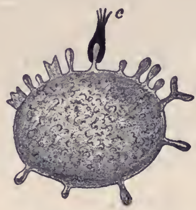


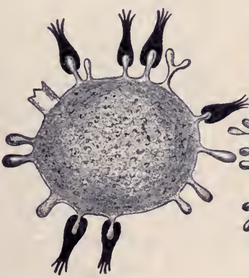
FIG. 70. FIG. 71.

FIGS. 70 AND 71.—CELLS WITH VARIOUS RECEPTORS OR HAPTOPHOROUS GROUPS OF THE FIRST ORDER.

(*a*) Adapted to combination with the haptophorous groups (*b*) of various chemical compounds brought to them. It will be noted that there is no mechanism by which the toxophorous elements of the molecules (*c*) can be brought to the cell.

traction) existing between phagocytic cells and micro-organisms. He divides such cells into two classes:

(1) *Microphages*—represented practically exclusively by the neutrophilic polymorphonuclear leukocytes.



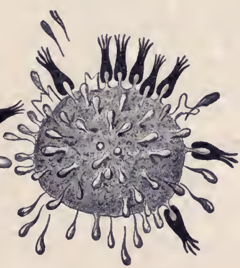


FIG. 72. FIG. 73.

FIGS. 72 AND 73.—SHOW THE REGENERATION OF THE CELL-HAPTOPHORES OR RECEPTORS TO COMPENSATE FOR THE LOSS OF THOSE THROWN OUT OF SERVICE.

(2) *Macrophages*—large mononuclear leukocytes, endothelial cells lining serous membranes, and fixed mononuclear cells of the spleen follicles and lymph sinuses.

The most active are the microphages, as they have the power of independent motion. When the bacteria gain entrance into the body the phagocytes are attached, and they attempt to ingest and destroy the invaders. If the immunity of the animal is marked, many of the organisms will be found within the cells; if the immunity is slight, few cells will contain bacteria. At one time it was claimed that phagocytes could take up only dead bacteria, but it has been demonstrated that the leukocytes can take up living organisms. As a rule, the bacteria

FIG. 74.—SHOWS THE NUMBER OF HAPTOPHORES REGENERATED BY THE CELL BECOMING EXCESSIVE, THEY ARE THROWN OFF INTO THE TISSUE JUICE.

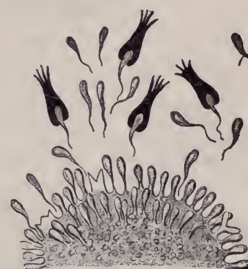


FIG. 75.—EXPLAINS WHAT ANTITOXINS ARE AND HOW THEY ARE FORMED.

The liberated receptors in the tissue juice and in the blood possess identical combining affinities with those upon the cell, and meeting the adapted haptophorous elements in the blood, combine with them, thus keeping them from the cells.

are ultimately destroyed, but on the other hand, the phagocyte may be the one to perish, and in this way permit a wide distribution of the invaders. Experiments have shown that the bacteria must be acted upon by a substance in the blood known as an *opsonin*, before the phagocyte is able to digest them.

4. Ehrlich's lateral chain theory. This receives its name from its analogy to the benzole ring in chemistry with the accompanying lateral chains. For convenience terms are used that can be applied to formed bodies, although they cannot be demonstrated as such in the body juices.

In this theory it is claimed that immunity depends upon the presence or absence of "receptors," the equivalent of the chemical lateral chains. The normal or fixed receptor is that body attached to the cell by means of which the cell is acted upon by various substances, nutritive or otherwise. Each receptor is supposed to be so formed as to unite with a certain body of a definite character. When the action of the bacteria upon the tissue cells is considered, it is supposed that the poisonous products consist of two portions, the "haptophorous"

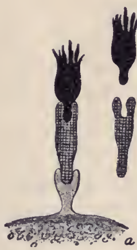


FIG. 76.—COMBINATION OF CELL (*a*), AMBOCEPTOR (*b*), AND COMPLEMENT (*c*).

The amboceptor may unite with the cell, but cannot affect it alone. The complement cannot unite with the cell except through the amboceptor, having no adaptation to the cell directly.

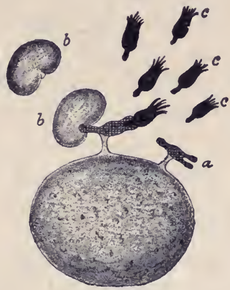


FIG. 77.

Cell with receptors of the second order (*a*) by which the cells fix useful molecules, of albumins, etc., on one hand (*b*), and zymogen molecules (*c*) on the other hand, and make use of the one substance through the action of the other.

and the "toxophorous" groups. The combination is thought to take place as follows: The haptophoric group unites with a certain definite receptor, and by so doing interferes with the normal function of the cell. At the same time the toxophoric group is able then to act directly upon the cell. If this group is very powerful the cell is destroyed, and if a sufficient number are involved the individual may die. When such a union occurs the receptors are of no further use. It has been found in such cases that in order to get back to the normal the cell will be so stimulated that new receptors similar to the ones destroyed will be formed. As a rule, a great excess of receptors

will result, and many of these will be cast forth into the circulation, becoming free receptors. These cast-off receptors are what constitute an antitoxin, and, on coming in contact with the toxin molecule, unite with the haptophorous portion and consequently render it harmless. It being attached to a free receptor, it is no longer able to combine with a fixed receptor.

In bacteriolysis and hemolysis, or cytolysis in general, conditions in which the destruction of actual cells is concerned, the destruction is brought about in a more complicated manner. Two other bodies than the cells are involved. One of these, known as the *complement*, is normally present in all serum. It is destroyed by a temperature of 55° C. for one-half hour, and is termed, therefore, thermolabile. The other, the *immune body*, or *amboceptor*, occurs in serum only as the result of the injection into the individual of the definite antigen. In other words, the amboceptor is specific in that it can combine only with that substance which gave rise to its formation. As it can resist heat up to 80° C., it is termed thermostabile. In order that the cell be destroyed the complement unites with the specific amboceptor, which in turn joins with the fixed receptor, and the destructive action then occurs.

In active acquired immunity against foreign cells the invaded animal forms large amounts of amboceptor, which, being free within the blood, unite with and destroy the invading cells. If the supply is sufficient, the individual will recover. In passive acquired immunity large numbers of amboceptors in the serum from the immunized animal are directly introduced into the patient, and in this way effect a cure.

Lysins are those antibodies that will cause the destruction of cells, and they receive various names, according to the type of cell acted upon. The destruction is known as *lysis*. *Cytolysin* is the general name of all the substances that destroy the cells. A *bacteriolysin* causes lysis of bacteria; a *hemolysin*, that of erythrocytes.

It has been found, for example, that a "hemolysin" can be produced by injecting defibrinated rabbit's blood into a guinea-pig. The serum of the guinea-pig will develop marked ability to dissolve blood-corpuscles from the rabbit. This action can

be destroyed by heating the serum to 56° C., but the serum can be reactivated by the addition of fresh normal serum, as in it will be found complement. The immune serum will contain the amboceptor or immune body.

A. Foreign cells, blood, bacteria, etc.

B. Heated immune serum containing amboceptor, but no complement.

C. Unheated normal serum containing complement, but no amboceptor.

A + B = No lysis.

A + C = No lysis.

A + B + C = Lysis.

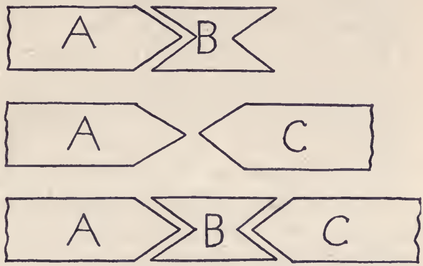


FIG. 78.—DIAGRAM REPRESENTING METHOD OF COMBINATION OF ANTIGEN (A), AMBOCEPTOR (B), AND COMPLEMENT (C) IN PRODUCING LYSIS.

In order to bring about the solution the three factors must be present. Experiments show that the complement cannot combine directly with the cell, but that there must be an intermediate substance, which is known as the amboceptor.

Agglutinins.—When bacteria or other cells are injected into the body there are formed within the serum definite substances, which when brought together with emulsions of the corresponding bacteria will cause the "clumping" or agglutination of the bacteria. If these are normally motile they will become less motile, and may lose that power entirely.

As the action is specific, it is commonly used for diagnostic purposes, especially in typhoid fever, when it is known as the "*Widal* reaction" (*q. v.*).

Precipitins.—It has been found that when an immune serum is brought together with a clear filtrate of a bouillon culture of the organism used for injection, there will appear a turbidity

which will collect gradually at the bottom of the test-tube as a precipitate.

Such substances are formed whenever foreign albumins, either of vegetable or animal origin, are introduced through parenteral channels. These bodies are called precipitins.

These precipitins are specific in their reaction, and have been used for the purpose of identifying the origin of various albumins. Under the term of the "biologic" blood-test this action has been employed in medicolegal cases to determine the source of blood-stains. It is also made use of in establishing zoölogic relationships between different animals.

If human blood is injected a number of times into a rabbit, the serum from the rabbit's blood will form a precipitate with normal human blood-serum when the two are mixed in a test-tube.

It is thought by some that the agglutinins and precipitins are practically similar substances; agglutination being a bringing together of cells; precipitin action, the bringing together of albuminous particles.

Anaphylaxis is a term applied to an increase of susceptibility to infection; it is the opposite of immunity. It is a reaction that will occur with the parenteral form of injection of foreign proteins of any kind. In order to obtain the characteristic reaction it is necessary that a period of from six to ten days intervene between the first and second injection. A guinea-pig may be sensitized by 0.001 gm. of horse serum introduced into the peritoneal cavity. Eight to ten days later a second injection of 0.1 gm. of the serum is given, at which time the animal will become restless, short of breath, scratch itself violently about the nose, then depressed, and dies within one hour. Autopsy shows the lungs to be greatly distended and numerous small hemorrhages present. Similar symptoms have been encountered in people who have received antitoxin horse serum. In addition, there are skin eruptions, joint-pains, and edema, a condition known as serum sickness.

The anaphylactic reaction is specific, and the susceptibility, once acquired, may continue throughout the life of the animal, and may be transmitted by the blood of the mother to the

offspring. It may be natural or acquired, active or passive. It may also be general or local.

The possibility of local anaphylactic reactions has been made use of in the diagnosis of various diseases, particularly tuberculosis. The subcutaneous injection of tuberculin in a non-tuberculous person will cause no disturbance. The same dose in the tuberculous will cause headache, muscle pains, fever, and local reddening around the site of inoculation. Similar results are obtained if the tuberculin is instilled in the eye (Calmette reaction), but as severe inflammations have been occasioned, the method is not recommended. A like reaction is claimed when luetin, a specially ground-up culture of the Treponema pallidum, is employed as a subcutaneous reaction for syphilis. Much experimentation is being done along this line in respect to the making of diagnoses in various diseases. The symptoms of many diseases may be due to the presence of foreign proteins that have sensitized the individual.

According to Vaughan, anaphylaxis results when the strange protein in the blood reaches the cells and is slowly broken down by enzymic action. The cells, having once acquired the property of destruction, seize eagerly upon the protein the next time it is offered, disintegrate it rapidly, and so disseminate throughout the body the disintegration products, some of which may be toxic and account for the reaction.

Complement Fixation.—The well-known *Wassermann test* for syphilis is nothing more than the application of the complement-fixation reaction to diagnostic purposes. It is a method of making the diagnosis of syphilis by demonstrating in the blood (or cerebrospinal fluid, milk, or urine) of the patient a complement-fixing substance not present in normal blood.

The test is twofold: (1) A combination of syphilitic antigen, complement, and suspected serum. (2) A subsequent addition to the mixture of blood-corpuscles and hemolytic amboceptor. If the suspected serum contain the syphilitic antibody, the antigen and the complement unite with it, and the complement being thus "fixed," no hemolysis can take place upon the subsequent addition of the blood-corpuscles and hemolytic serum. If, on the other hand, the suspected serum contain no

antibody, the complement cannot be fixed, and is, therefore, free to act upon the subsequently added blood-corpuscles in the presence of the hemolytic serum, and hemolysis results.

It is thus seen that the first test is made for the purpose of fixing the complement, and the second for the purpose of finding out whether or not it has been fixed.

The materials required for the Wassermann test are as follows:

A. Fresh sheep red blood-cells that have been thoroughly washed so as to get rid of any complement.

B. Blood-serum from a rabbit that has been immunized against the blood-cells of a sheep.

C. Immunized rabbit serum (B) that has been heated to 56° C. for thirty minutes in order to destroy the complement, but not affecting the specific amboceptor or immune body which can resist such a temperature.

D. Normal serum from a guinea-pig containing complement.

E. Antigen. Extract of the liver of a syphilitic fetus in alcohol, ether, or water; or lecithin, cholesterin, or extracts from organs of non-syphilitics.

F. Fluid suspected to contain syphilitic antibody (amboceptor). This should be heated to 56° C. for one-half hour to destroy the complement.

For the actual performing of the test there are also needed:

E 1. Serum from a known case of syphilis, containing, therefore, the syphilitic amboceptor. This also must be heated.

E 2. Serum from a known non-syphilitic.

Before using the solutions in the hemolytic series (C and D) they must be carefully standardized, so as to determine just what amount of amboceptor and of complement are necessary in order to cause hemolysis exactly. Such an amount is called a unit.

D, complement + E, syphilitic antigen + F, suspected fluid	Incubated for one hour at 37° C. Then add	A, sheep corpuscles + C, hemolytic amboceptor

The combination of the two systems is placed in an incubator

at 37° C. for one hour, then put in the ice-box for twenty-four hours, at the end of which time the final conclusions are drawn.

If F contains the syphilitic amboceptor, it will combine with both D, complement, and E, the syphilitic antigen. Consequently, when A and C of the hemolytic system are added, it will be found that the complement D has been already used or fixed. Therefore no free complement is present to unite with A and C and cause hemolysis. *A positive Wassermann is indicated by the absence of hemolysis.*

If F does not contain syphilitic amboceptor the complement D will remain free, and when A and C are added, it will combine and cause the destruction (hemolysis) of the sheep corpuscles (A). *A negative Wassermann, therefore, is indicated by the presence of hemolysis.*

When there is no hemolysis the blood-cells will be in the bottom of the test-tube, and the liquid will be clear and colorless. In hemolysis there may be either a complete or a partial destruction of the red cells, and the overlying fluid will be of a reddish color, the degree depending upon the amount of cellular disintegration.

E 1 and E 2 are employed as controls in the series of tests necessary to determine the accuracy of the solutions that are used in the reactions above mentioned.

A positive Wassermann is nearly conclusive of there being a syphilitic infection. In active syphilis positive reactions have occurred in as much as 94 per cent. of the cases; in latent syphilis, 50 per cent.; and in chronic diseases of the nervous system, as general paresis and tabes dorsalis, the figures vary from 90 per cent. in the first to 50 per cent. in the latter.

On the other hand, a negative Wassermann does not exclude syphilis, as the result may be due to the treatment; as under active treatment with mercury and the iodids, salvarsan, or neosalvarsan the reaction is usually negative.

Antitoxin Manufacture.—As has been stated, if small doses of some special poison, such as diphtheria toxin, be repeatedly injected into a susceptible animal in increasing amount there will be developed in the blood-serum of that animal an antibody, called an antitoxin. This is formed by the cells and, according

to Ehrlich's side-chain theory, corresponds to the free receptors. By injecting the antitoxin into an immunized animal it can resist a dose of toxin that ordinarily would be several times more than necessary to kill. That a combination occurs between the toxin and antitoxin can be proved by mixing the two together in a test-tube. The resulting mixture will prove harmless when injected into a susceptible animal.

Antitoxins are destroyed by heat, acids, and many chemicals, and gradually deteriorate spontaneously when in solution, particularly when kept at room-temperature. To preserve their activity the temperature should be not more than 5° C. Antitoxins are specific in that they neutralize the corresponding toxin and have no other apparent action within the body. The occasional ill effects, such as serum sickness, following the injection of antitoxic serums are due to other substances (the proteins in the serum) and not to the antitoxins themselves. Antitoxins may be injected subcutaneously, intravenously, into the subarachnoid space, into a nerve, into the brain substance, or into any of the body cavities. They are practically useless when given by the mouth, as very little is absorbed. As antitoxins, when injected into an organism, tend to disappear rather quickly, passive or antitoxic immunity is, therefore, transient; it cannot be depended upon for more than ten days or two weeks. When antitoxic serum is injected subcutaneously the antitoxin is absorbed slowly, requiring about forty-eight hours before it appears in the blood in maximum amount. When very prompt action is necessary the antitoxin should be introduced directly into the circulation by intravenous injection. Antitoxins are valuable both as curative and immunizing agents. For curative purposes they should be given early and in large enough doses to get their action before damage has been done by the toxins.

Preparation of Diphtheria Antitoxin.—As similar methods are used for practically all types of toxins, a description of the preparation of diphtheria antitoxin will be sufficient.

To obtain the necessary toxin virulent diphtheria bacilli are grown in alkaline bouillon containing 0.2 per cent. dextrose at a temperature of 37° C. for five to seven days. The

bouillon culture is then passed through a porcelain or Berkefeld filter and stored in sterile containers in an ice-box. On account of general convenience horses are commonly employed. They should be perfectly healthy, free from glanders, tuberculosis, or tetanus. The horse is injected hypodermically with 0.1 c.c. of the toxic filtrate. This is frequently followed by a rise in temperature, local reaction, and some general disturbance. When these disappear, a second dose is given. The doses are cautiously increased in amount and administered every few days until from 500 to 1000 c.c. of the toxin can be given without effect. When the degree of immunity is sufficiently high, blood is drawn from the jugular vein to the amount of from 3 to 9 liters, according to the size of the horse, collected in sterile bottles, then placed on ice for several days until the clear serum separates from the clot. This is then drawn off from the coagulated blood under aseptic precautions, and in it is the antitoxin. It is preserved by the addition of small amounts of phenol, trikresol, etc.; this latter seems to be the most satisfactory. After the serum has been obtained, its strength or potency, as expressed by the term "immunizing units," must be determined. An antitoxic unit may be defined as being *ten times the least quantity of antitoxic serum that will protect a standard* (300-*gm.*) *guinea-pig against ten times the least certainly fatal dose of toxic bouillon.*

To determine the strength of any given serum, the minimum fatal dose of a sterile toxin for a 300-gm. guinea-pig must be ascertained. Then must be determined the least quantity of antitoxic serum that will protect a guinea-pig against ten times the ascertained minimum fatal dose of the toxin. The necessary dose of antitoxic serum is expressed as a fraction of a cubic centimeter and multiplied by 10, the result equaling one unit.

Ehrlich, in determining the unit, makes use of a standard antitoxin (antitoxins not deteriorating or varying as do toxins) by which the antitoxin combining power of the test toxic bouillon is first determined. The toxin unit (*the smallest amount of toxin required to kill a guinea-pig weighing* 300 *gm.*), having been found, is then used to determine the antitoxic unit of antitoxins of unknown strength.

The power of antitoxic serums differ greatly: some contain 200 to 300 units per cubic centimeter, while others may contain even 1700 to 2000 per cubic centimeter.

Inasmuch as the antitoxin is only a small portion of the serum, various methods have been sought, by means of which the useless, and sometimes harmful, portions may be eliminated. The method employed at present in order to obtain such a concentrated antitoxin is that elaborated by Gibson—that of globulin precipitation.

Tetanus Antitoxin.—The method of obtaining is similar to that employed for securing the diphtheria antitoxin, the unit, however, being somewhat different. The use of this antitoxin has not been as satisfactory as that of diphtheria, on account of the rapidity with which the central nerve-cells combine with the tetanus toxin and the firmness of that union. Consequently, as a curative after toxic symptoms have developed, it is not very efficient, athough more cases of tetanus do recover after antitoxin treatment than after any other form. Its chief value is as a preventive. It should be given as soon as possible after the injury has been received, in order that the free receptors will be present ready to combine with the toxin as soon as it has formed. By means of this prophylactic dose of antitoxin the number of fatal cases of tetanus infection following injuries received on the 4th of July has decreased very greatly.

Bacterination (bacterial vaccine) refers to the introduction within the body of measured amounts of sterile cultures of bacteria, in order that the individual may develop an immunity to that particular organism. This method has been employed in the infections of many varieties of bacteria, with particularly favorable results where the cocci have been the invaders. In pyorrhea alveolaris much success has been attained.

Two types of bacterins (vaccines) are employed, the *stock* vaccine and the *autogenous* vaccine. In the latter the bacterin is obtained by the cultivation of the organisms present in the lesion of the infected person. The stock vaccine is made of bacteria similar to those in the infected individual, but obtained from some other source. As a rule, better results are obtained by using the autogenous cultures, although in gonococcal infec-

tions the stock bacterin seems to be more satisfactory in many instances.

Preparation of a Bacterin.—The vaccine is usually prepared from a fresh twenty-four-hour growth of a pure culture of the micro-organism on an agar slant. The growth is scraped off and made into an emulsion with physiologic salt solution. The emulsion is then sterilized by heating at 60° C. for one hour and afterward is further diluted. This is done so that 1 c.c. will represent approximately the dose to be given. This dilution will vary, as the number of bacteria to a dose varies according to the organism used. Culture-tubes are inoculated with the vaccine and incubated for twenty-four hours at 37° C. to make sure that the sterilization was complete. To preserve the bacterin, 0.5 per cent. of carbolic acid or trikresol is used.

The injections should always be given subcutaneously. Usually three or four injections are given at intervals of from five to ten days, as in this way an immunity of much higher grade and longer duration is obtained. In most instances the acquired immunity lasts from two to five years and may be renewed.

Preventive inoculations with bacterial vaccines have been used extensively against typhoid fever, plague, and cholera.

The bacterins are used also as curative agents, but much care should be observed in giving the proper dosage. A minimum amount should be given, and if it creates no unfavorable reaction, a larger amount should be given subsequently.

Opsonins.—It has been shown that in the serum of persons convalescent from infectious diseases or vaccinated (by bacterins) against certain infectious diseases substances are present which prepare the micro-organisms for the action of the phagocytes. These substances are termed *opsonins.* If fresh blood is mixed with an emulsion of some bacteria, and then incubated for one-half hour, it will be found that many of the bacteria are within the polymorphonuclear leukocytes. If the serum is washed away from the leukocytes before adding the bacteria, none of the latter will be found within the leukocytes. In order to show that this effect is on the bacteria rather than on the leukocytes, the bacterial suspension may be treated with some

serum for one-half hour, then washed free from this serum by means of salt solution and a centrifuge, and then mixed with some serum-free leukocytes; then it will be found that phagocytosis occurred as before.

The estimation of the opsonic power of the serum has been attempted and various methods elaborated. It may be questioned, however, whether any of the tests now in use is a true index of the amount of opsonins in the serum, although it may be taken to indicate roughly the measure of their activity.

CHAPTER XII

BACTERIA

These organisms are of interest in that they may be parasitic upon and within the body of man, of the lower animals, and other plants. The less important ones will be presented first, the bacteria being discussed more fully later; these latter being especially important on account of their relation to disease and their bearing upon general hygiene and preventive medicine.

THE YEASTS

The yeasts, *blastomycetes* or *saccharomycetes*, are unicellular fungi which multiply by budding, in which naked asci (spore cases) are formed freely on the mycelium. The yeast cell is, as a rule, oval, but among the wild-yeasts, or torulæ, spheric forms are common. Great variations occur in size, yeasts measuring usually from 10 to 20 μ in length, with a width of about one-half or two-thirds of the long diameter. They possess a well-defined, doubly contoured cell-membrane, composed chiefly of cellulose, and the cytoplasm, unlike that of the bacteria, shows definite structure. These organisms multiply by *budding*, at which time the mother-cell sends out a small globular projection of the cell membrane into which maternal cytoplasm flows. This bud gradually enlarges until it becomes about the same size as that of the original cell. Finally, by the gradual narrowing of the isthmus connecting the two, the daughter-cell becomes complete and free. When the surrounding conditions are unfavorable most yeasts are able to form spores. These, called "ascospores," are formed within the yeast cell itself, each spore forming a separate membrane of its own, but all of them lying well protected within the original cell-membrane.

In this family Besson includes the following parasitic yeasts: the *Endomyces albicans* (*Oïdium albicans*), the parasite of *thrush;* the *Cryptococcus dermatitis* (*Blastomyces dermatitis*), the cause of a form of chronic dermatitis; and the *Saccharomyces tumefaciens.*

THE MOLDS

In this group, the *hyphomycetes,* may be included many organisms having in common the formation of a well-marked mycelium, but differing so greatly in other respects as to be placed in widely separated groups in the systematic arrangement of the fungi. The characteristic feature of this class is the formation of long, interlacing filaments or threads, known as mycelia. From these there extend branches called hyphæ. In this class may be placed the *Achorion schönleini* (the parasite causing *favus*), the *Trichophyton* and *Microsporon,* the *Mucor,* the *Aspergillus,* and *Eurotium.* These parasitic organisms are described in detail under the headings of the diseases caused by them.

THE HIGHER BACTERIA

This group occupies an intermediate position between the true bacteria and the molds. These organisms are characterized by filamentous forms with real or apparent branchings. The filaments are usually divided transversely, appearing as if composed of bacilli. The free ends only seem to be endowed with the ability to reproduce, and they develop peculiar elements that differentiate the higher from the other bacteria, whose cells are all equally free and independent.

Leptothrix.—These comprise long threads which do not branch, and are at times separated with difficulty from chains of bacilli. They rarely cause trouble, but have been observed in connection with inflammations of the mouth and pharynx, particularly along the edges of the tonsillar crypts, where they grow with the formation of persistent white patches. Cultivation of the leptothrix is difficult.

Cladothrix is a thread-like form in which false branching may be recognized, an appearance resulting from the fragmentation of the threads. The terminal cell breaks away

from the main stem, is set at an angle by the elongation of the thread itself, and, as both continue to divide, the simulation of true branching is produced. This type is probably not pathogenic; most of the cases ascribed to this class were likely due to streptothrix infection.

Streptothrix denotes forms with numerous true branches and spores which usually appear in chains. Numerous cases of disease have been reported as being caused by these organisms.

Actinomyces is characterized by the formation of club-shaped ends and the radiating arrangement of the threads. This organism causes a specific disease of the lower animals, sometimes transmitted to the human being.

BACTERIA

Bacteria are minute unicellular organisms, probably belonging to the vegetable kingdom, the *schizomycetes*. It is difficult to classify them, but probably the best arrangement is a modification of Migula's method as follows:

CLASSIFICATION OF THE BACTERIA

I. ORDER: EUBACTERIA (True Bacteria)

A. Sub-order: Haplobacteria (Lower Bacteria)

I. Family Coccaceæ. Cells globular, becoming slightly elongate before division. Division in one, two, or three directions of space. Formation of endospores very rare.
- (A) Without flagella.
  1. *Streptococcus*. Division in one direction of space, producing chains like strings of beads.
  2. *Micrococcus*. Division in two directions of space, so that tetrads are often formed.
  3. *Sarcina*. Division in three directions of space, leading to the formation of bale-like packages.
- (B) With flagella.
  1. *Planococcus*. Division in two directions of space, like micrococcus.
  2. *Planosarcina*. Division in three directions, like sarcina.

II. Family Bacteriaceæ. Cells more or less elongate, cylindric, and straight. They never form spiral windings. Division in one direction of space only, transverse to the long axis of the cell.
- (A) Without flagella.
  1. *Bacterium*. Occasional endospores.
- (B) With flagella.

2. *Bacillus.* Flagella arising from any part of the surface. Endospore formation common.
3. *Pseudomonas.* Flagella attached only at the ends of the cell. Endospores very rare.

III. Family SPIRILLACEÆ. Cells twisted spirally like a corkscrew, or representing sections of the spiral. Division only transverse to the long diameter.

1. *Spirosoma.* Rigid; without flagella.
2. *Microspira.* Rigid; having one, two, or three undulating flagella at the ends.
3. *Spirillum.* Rigid; having from five to twenty curved or undulating flagella at the ends.
4. *Spirochæta.*[1] Serpentine and flexible. Flagella not observed; probably swim by means of an undulating membrane.

B. SUB-ORDER: Trichobacteria (Higher Bacteria)

IV. Family MYCOBACTERIACEÆ. Cells forming long or short cylindric filaments, often clavate-cuneate or irregular in form, and at times showing true or false branchings. No endospores, but formation of gonidia-like bodies due to segmentation of the cells. No flagella. Division at right angles to the axis of rod in filament. Filaments not surrounded by a sheath as in Chlamydobacteriaceæ.

1. *Myobacterium.* Cells in their ordinary form, short cylindric rods often bent and irregularly cuneate. At times **Y**-shaped forms or longer filaments with true branchings may produce short coccoid elements, perhaps gonidia. (This genus includes the Corynebacterium of Lehmann-Neumann.) No flagella.
2. *Actinomyes.* Cells in their ordinary form as long branched filaments; growth coherent, dry, or crumpled. Produce gonidia-like bodies. Cultures generally have a moldy appearance, due to the development of aërial hyphæ. No flagella.

V. Family CHLAMYDOBACTERIACEÆ. Forms that vary in different stages of their development, but all characterized by a surrounding sheath about both branched and unbranched threads. Division transverse to the length of the filaments.

1. *Cladothrix.* Characterized by pseudodichotomous branchings. Division only transverse. Multiplication by the separation of whole branches. Transplantation by means of polar flagellated swarm-spores.
2. *Crenothrix.* Cells united to form unbranched threads which in the beginning divide transversely. Later the cells divide in all three directions of space. The products of final division become spheric, and serve as reproductive elements.
3. *Phragmidiothrix.* Cells at first united into unbranched threads. Divide in three directions of space. Late in the development, by the growth of certain of the cells through the delicate, closely approximated sheath, branched forms are produced.

[1] The spirochæta and some closely related forms are now thought to be more properly classified among the protozoa than among the bacteria.

4. *Thiothrix.* Unbranched cells inclosed in a delicate sheath. Non-motile. Division in one direction of space. Cells contain sulphur grains.

II. ORDER: THIOBACTERIA (Sulphur Bacteria)

I. Family BEGGIATOACEÆ. Cells united to form threads which are not surrounded by an inclosing sheath. The septa are scarcely visible. Divide in one direction of space only. Motility accomplished through the presence of an undulating membrane. Cells contain sulphur grains.

There are two families, numerous subfamilies, and thirteen genera in this order. They are all micro-organisms of the water and soil, and have no interest for the medical student.

A more common but less accurate method of classification divides bacteria into:

1. *Bacillus.*—A rod-shaped organism that is not curved or twisted upon itself, one diameter being distinctly greater than the other.

2. *Micrococcus or Coccus.*—A minute spheric organism.

(*a*) *Diplococcus*, when occurring in twos.

(*b*) *Streptococcus*, when occurring in chains.

(*c*) *Staphylococcus*, when in bunches like grapes.

(*d*) *Tetracocci*, when division takes place in two directions, and the individuals remain attached in groups of four.

(*e*) *Sarcina*, when dividing in three directions, giving rise to bale-like packages.

(*f*) *Zoöglea*, when grouped in irregular masses.

3. (*a*) *Spirillum.*—An organism twisted like a corkscrew and rigid; usually has polar flagellæ.

(*b*) *Spirochæta*, when the organism is long, slender, flexible, and without flagella.

(*c*) *Vibrio.*—A short organism, bent like a comma, usually with a single end-flagellum.

Structure.—Bacteria are composed of a small amount of cytoplasm surrounding a large but indistinctly defined nucleus. In this cytoplasm may be found granules of fat, pigment, sulphur, etc. Each cell is surrounded by a distinct cell-wall, and sometimes there is present a peculiar gelatinous material forming a capsule.

Motility.—The greater number of bacteria are non-motile, but many possess the power of motility as a result of the

presence of flagella. Most of the cocci are non-motile. According to the presence or absence of flagella, the following classification of bacteria has been made:

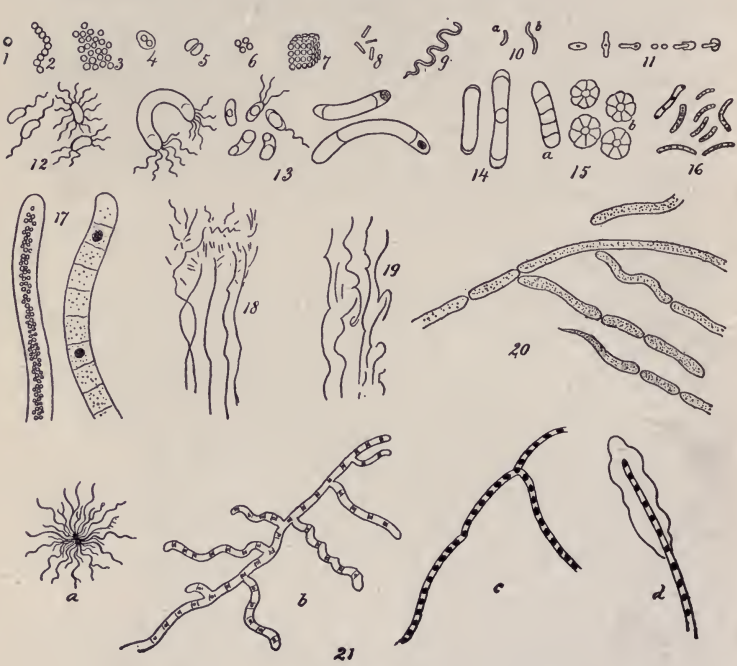


FIG. 79.—TYPES OF MICRO-ORGANISMS.

1, Coccus; 2, streptococcus; 3, staphylococcus; 4, capsulated diplococcus; 5, biscuit-shaped coccus; 6, tetrads; 7, sarcina form; 8, types of bacilli (1 to 8 are diagrammatic); 9, non-septate spirillum (× 1000); 10, ordinary spirillum: (*a*) comma-shaped element; (*b*) formation of spiral by comma-shaped elements (× 1000); 11, types of spore formation; 12, flagellated bacteria; 13, changes in bacteria produced by plasmolysis (after Fischer); 14, bacilli with terminal protoplasm (Bütschli); 15, (*a*) Bacillus composed of five protoplasmic meshes; (*b*) protoplasmic network in micrococcus (Bütschli); 16, bacteria containing metachromatic granules (Ernst Neisser); 17, Beggiatoa alba—both filaments contain sulphur granules—one is septate; 18, Thiothrix tenuis (Winogradski); 19, Leptothrix innominata (Miller); 20, Cladothrix dichotoma (Zopf); 21, Streptothrix actinomyces (Boström): (*a*) colony under low power; (*b*) filament showing true branching; (*c*) filament containing coccus-like bodies; (*d*) filament with club at end.

1. *Gymnobacteria*, forms without flagella.

2. *Trichobacteria*, forms with flagella.

(*a*) *Monotricha*, a single flagellum at one end.

(*b*) *Leptotricha*, a bundle of flagella at one end.

(*c*) *Amphitricha*, a flagellum at each end.

(*d*) *Peritricha*, flagella arising from all parts of the surface of the organism.

Size.—Bacteria are so minute that a special unit has been adopted for their measurement. This is the micromillimeter (μ), or one-thousandth part of a millimeter, known as the *micron*. It is equivalent to the one-twenty-five-thousandth part of an inch. The size of bacteria vary from a fraction of a micromillimeter to 20 or even 40 micromillimeters.

Reproduction.—*Fission.*—The most common method in which the organisms divide into two. This occurs very rapidly if there is enough nutritive material present and the surrounding conditions are favorable, the length of a generation varying from fifteen to forty minutes.

Sporulation occurs when the conditions do not favor multiplication. There are then formed small, round or oval, highly refracting bodies called *spores*, which are capable of resisting very unfavorable surroundings. They differ from bacteria in being able to withstand evaporation and exposure to quite high degrees of heat. Few adult bacteria can resist temperatures above 70° C., but spores are uninjured by such heat and may even resist the temperature of boiling water (100° C.) for a short time. If the spore develops within the bacterium in the middle, or at one or other of the ends, it is called an *endospore*. If the spore is so large as to cause a bulging of the organism it is called a *clostridium*. These forms occur in the bacilli. Among the micrococci there are times when the entire organism is transformed into a spore, an *arthrospore*.

Germination of Spores.—When conditions become favorable the spore may develop into an adult organism. Its contents, which have been clear and transparent, become granular, the body increases slightly in size, the capsule becomes less distinct, and in the course of time splits open to allow the escape of the young organism. This begins to increase in size, devel-

ops its characteristic capsule, and presently begins to multiply by fission.

Growth of Bacteria.—In the cultivation of bacteria there are many conditions that can influence the growth favorably or unfavorably. There are, however, certain factors that are really essential.

Food.—Bacteria grow best when diffusible albumins are present, but carbohydrates will do. It has been found that the food requirements differ very greatly with the different kinds of organisms. Some will live in water to which an extremely small amount of organic matter has been added. Others require a concentrated medium such as blood-serum. Then, too, the addition of certain substances, such as glucose or glycerin, may exert a very favorable influence.

Oxygen.—All micro-organisms must have oxygen in order to continue to live, but it may be present either in the free or in a combined condition. Those organisms which grow in the presence of free (uncombined) oxygen are known as *aërobes*. Those which will not grow in the presence of free oxygen are the *anaërobes*. There are, however, some of the aërobic type which will grow about as well without free oxygen as with it; these are the *optional* (facultative) *anaërobes*.

Moisture to some degree is an absolute necessity, but it may be present in very slight amount. Unless some is present nearly all organisms will dry up and cease to multiply, but spores may be formed first and persist more or less indefinitely. In making up artificial culture-media there should be present at least 80 per cent. of water.

Temperature of a proper degree is of the greatest importance. Every micro-organism grows best at some definite degree of heat, and shows variations in its activity as the temperature changes. The organisms, however, may be able to endure extreme degrees of cold without being destroyed—some can be placed in liquid air and yet undergo multiplication when the temperature is raised. They cannot, as a rule, stand the higher temperatures as well, although a few varieties of organisms may thrive at high degrees (65°–70° C.). They are called *thermophilic*, and are found in manure piles and hot springs.

The temperature at which micro-organisms grow best is known as the *optimum;* the lowest temperature at which they continue to multiply, as the *minimum;* the highest at which they remain active, the *maximum.* With pathogenic or disease-producing organisms the optimum temperature is that normal to the body (37° C.).

A temperature of from 50° to 60° C. will weaken and finally destroy nearly all forms. If they are exposed to steam or boiling water at the temperature of 100° C. all fully developed bacteria will be killed in a few minutes, but their spores may be able to resist this heat for a longer time. When dry heat is used a higher temperature is required. The spores may withstand 150° C. for an hour or 175° C. for five to ten minutes.

Reaction.—Most true bacteria grow best in neutral or feebly alkaline media, although some grow well in strong acids and others in marked alkalinity.

Many chemical bodies will restrain the growth or destroy the bacteria. These substances may be produced by the bacteria in their growth or they may be artificially introduced. Those which will restrain the growth but not kill are called *antiseptics;* those that kill, *germicides.*

Light, particularly the direct rays of the sun, will retard bacterial growth and in many cases kill the organisms. Certain colors distinctly retard growth, blue being the most effective. A weak, diffused light seems most favorable, but various organisms react differently, certain bacteria producing color only when exposed to the ordinary light of a room, while others will produce color only in the dark.

Motion.—Bacteria apparently grow best when there is an absence of motion.

Electricity and *x-rays* do not seem to have any constant effect upon bacteria.

Symbiosis, or the association of one organism with another, may cause an increase in its activity, as the growth of the tetanus bacillus in the presence of other bacteria that use up the supply of oxygen. *Antibiosis* is the condition in which the association may be detrimental to one of the organisms.

Products of Bacterial Growth.—According to the substances formed as a result of their growth bacteria may be divided into:

Zymogens, bacteria of fermentation.

Saprogens, bacteria of putrefaction.

Chromogens, bacteria which produce colors.

Photogens, phosphorescent bacteria.

Aërogens, gas producers.

Pathogens, bacteria which produce disease.

Bacteria through their activity split up complex organic substances into simple compounds.

Fermentation is the splitting up of carbohydrates by the activity of the micro-organisms. This is the process that takes place in the formation of alcohol as a result of the action of yeast. Other forms of fermentation are those in which acetic, lactic, or butyric acids result.

Putrefaction is the breaking up of nitrogenous compounds by micro-organisms that can live only in dead organic substances. The albumins are first transformed into peptones, which split up into gases, acids, bases, and salts.

The albumins may become changed to toxalbumins or into alkaloidal substances called *ptomains*, which are "chemical compounds, basic in character, formed by the action of bacteria upon organic matter." Ptomains are generally formed outside of the living body and cause harm only when introduced within it.

Toxins and *toxalbumins* are poisonous substances elaborated by bacteria during growth, and it is upon them that the disease-producing power of the organism rests.

The *bacterioproteins* also belong to this same group. These bacterial products are destroyed by sunlight, by heating to 60° to 80° C., by long keeping, and by the gastric juices. Tuberculin is an exception, in that it remains unaltered at a temperature of 100° C. The poisonous bodies may be either soluble or insoluble, and are generally peculiar to the variety of organism by which they are formed. Certain ones select definite cells upon which they act, and are called *specific*. Others, having no special selective powers, are *non-specific*.

Chromogenesis.—Bacteria that produce colored colonies or give a color to the medium in which they grow are called *chromogenic;* those producing white or no color, *non-chromogenic.* Most chromogenic organisms are saprophytic and non-pathogenic; but some of the pathogenic forms may produce color. Almost all known colors may be formed by different bacteria, and sometimes one organism will form two or more colors. The formation of the pigment probably depends upon the presence of oxygen.

Aërogenesis.—During fermentation and decomposition various gases are given off, such as carbon dioxide, sulphureted hydrogen, ammonia, etc.

Other enzymes formed by bacteria may cause the coagulation of milk and the liquefaction of gelatin. Some bacteria liquefy the gelatin in such a peculiar and characteristic manner as to make the appearance a valuable guide for the differentiation of species.

Pathogenesis.—Those micro-organisms which cause disease are called *pathogenic;* those that do not, *non-pathogenic.* There is, however, no sharp line between the two, as under adverse cultural conditions the pathogens may lose their ability to produce disease. On the other hand, those that are usually harmless may be made virulent.

CHAPTER XIII

SPECIFIC MICRO-ORGANISMS

Staphylococcus pyogenes aureus is a non-motile, facultative, anaërobic coccus about 0.8 μ in diameter, occurring in groups or singly.

Stains with aqueous solutions of anilin dyes and by Gram's method.

It gives rise to pus-formation and to pyemia.

Culture.—On gelatin plates occurs as small orange-colored colonies, which cause liquefaction on the surface. The orange pigment is best seen in the center of the colony. In gelatin puncture it grows as a fine white line, developing its pigment in about three days. Liquefies the gelatin and gives an orange-colored precipitate. On agar there is considerable variation in the color; is rarely golden, commonly yellow, often cream color. Grows as a moist, shining, circumscribed colony; does not liquefy agar. On potato growth is luxuriant. Best temperature, 37° C.

Staphylococcus pyogenes albus is similar in every respect except that it does not produce any pigment.

Staphylococcus epidermidis albus is a micrococcus constantly present in the skin. Thought to be the S. pyogenes albus in an attenuated condition. Similar to the above.

Staphylococcus pyogenes citreus, similar, except that it produces a lemon-yellow pigment.

Streptococcus pyogenes is a non-motile, non-liquefying, facultative anaërobic coccus that is about 0.4 to 1 μ in diameter, that occurs in chains of 10 to 50 members.

Stains with ordinary dyes and by Gram's.

Is found in pus and in erysipelas.

Culture.—Best at 37° C. On gelatin plates small, colorless, transparent colonies develop in from twenty-four to forty-

eight hours. Are round, granular, with raised edges. Do not liquefy. On agar-agar have very delicate, transparent colonies that do not coalesce.

When it gains entrance into the body it gives rise to more diffuse and more severe suppurations than does the staphylococcus.

Bacillus pyocyaneus is an actively motile, flagellated, facultative anaërobic, liquefying bacillus. Is rather short and slender, $0.3\,\mu \times 1$ to $21\,\mu$.

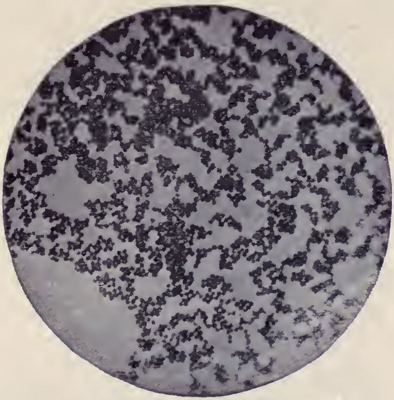


FIG. 80.—STAPHYLOCOCCUS PYOGENES AUREUS, FROM AN AGAR-AGAR CULTURE. $\times$ 1000 (Günther).

Stains.—Ordinary methods, but decolorized by Gram's. Is found in pus.

Culture.—On gelatin plates forms small, irregular, slightly greenish colonies. Produces a fluorescence of the neighboring gelatin. On agar-agar there is first produced a soluble bright green pigment along the line of inoculations. As the culture becomes older a second pigment forms, causing the medium to become a deep blue-green or dark blue.

Micrococcus gonorrhœa is a non-motile, non-liquefying coccus found in pairs with slightly concave surfaces opposed. From 0.8 to $1.5\,\mu$ in diameter.

Is a purely parasitic organism; is pathogenic for man only.

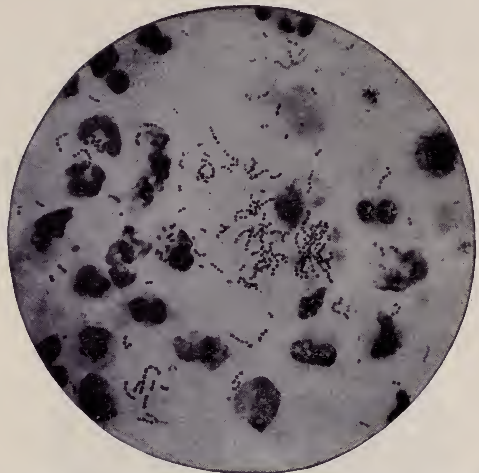


FIG. 81.—STREPTOCOCCUS PYOGENES, FROM THE PUS TAKEN FROM AN ABSCESS. × 1000 (Fränkel and Pfeiffer).

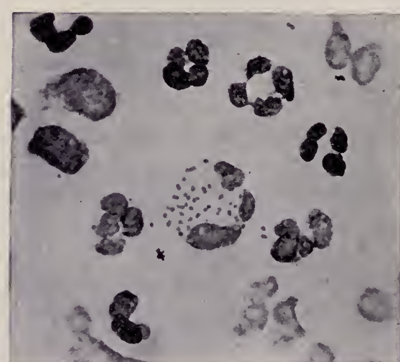


FIG. 82.—MENINGOCOCCUS IN SPINAL FLUID (from Hiss and Zinsser, "Text-Book of Bacteriology," D. Appleton & Co., Publishers).

Is found in the pus of gonorrhea, in the cells and also free in the serum.

Stains by ordinary methods but not by Gram's.

Culture.—Is difficult. Does not grow on any of the ordinary media. Human blood-serum is the best. On it the organism in about twenty-four hours forms isolated, thin, gray colonies that later on become confluent. Can be grown on gelatin that contains acid urine and also in plain acid urine.

It gives rise to suppurative inflammations of the mucous and serous membranes. May cause malignant endocarditis, arthritis, and salpingitis.

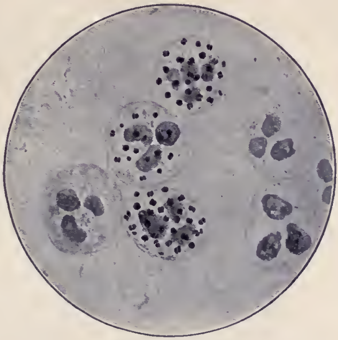


Fig. 83.—Gonococci in Urethral Pus (McFarland).

Diplococcus intracellularis meningitidis is a non-motile, non-liquefying, optionally anaërobic coccus, found usually in pairs, but may occur in short chains.

Is found within the protoplasm of the leukocytes.

Stains.—Ordinary ones and Gram's.

Culture.—Grows best at 37° C., but is not easily cultivated. Will develop on agar-agar, glycerin-agar, and in Loeffler's blood-serum. Growth is not characteristic; occurs as minute round grayish colonies that may coalesce. Requires frequent transplanting.

Diplococcus pneumoniæ is a minute, slightly lancet-shaped, non-motile, non-liquefying, optionally anaërobic diplococcus. Usually occurs in pairs, surrounded by a capsule that is not present when the organism is grown on culture medium.

Is found in the sputum of lobar pneumonia, in the exudate of meningitis, and sometimes in the saliva of healthy people. Is the common cause of croupous pneumonia, but is also found in inflammations of the serous membranes.

Stains.—Ordinary methods and Gram's.

Culture.—Grows best at 37° C., but has a range from 24° to 42° C. Will grow upon all culture media except potato. Gelatin plates (15 per cent. gelatin) give colonies that are small, round, circumscribed white points. On agar-agar the growth is almost invisible.

Bacillus tetani is a motile, flagellated, sporogenous, liquefying, obligatory anaërobic bacillus. Is found in earth,

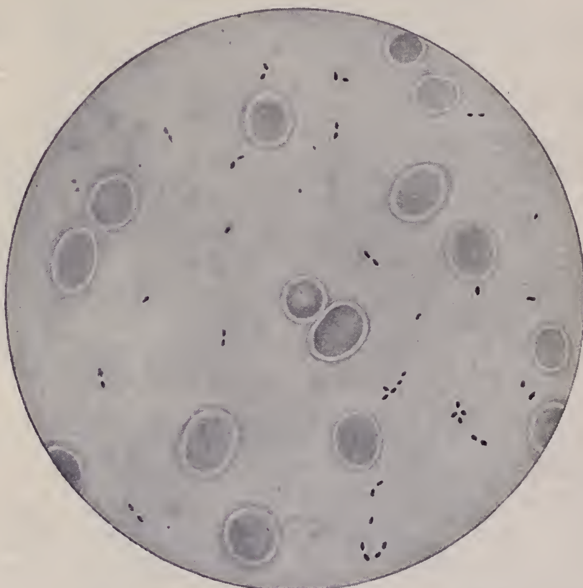


Fig. 84.—Capsulated Pneumococci in Blood from the Heart of a Rabbit. × 1000 (McFarland).

particularly that which has been manured, and in the discharges from wounds after infection. It is about 0.3 μ × 2 to 4 μ in size, usually straight, but frequently club-shaped, due to the presence of a large round spore.

Stains.—Usual ones and Gram's.

Culture.—Will grow only when there is no free oxygen present. Grows best in alkaline gelatin that contains 2 per

cent. dextrose. In stab cultures in gelatin and in agar-agar colonies form at right angles to the puncture. In gelatin liquefaction begins in the second week.

This organism is the cause of tetanus in man.

B. pneumoniæ is an encapsulated, non-motile, non-sporogenous, aërobic bacillus, so short that it may resemble a coccus. Varies, however, in length and sometimes occurs in chains of four or more individuals. Is found in the sputum and in the lung of croupous pneumonia.

Stains.—Ordinary methods, but not by Gram's.

Bacillus tuberculosis is non-motile, non-flagellate, non-sporogenous, non-liquefying, non-chromogenic, non-aërogenic, distinctly aërobic, and acid resisting. It commonly occurs in the form of slender, slightly curved rods with rounded ends, not infrequently showing branches. For this reason it may not be a bacillus, but an organism belonging to the higher bacteria. It measures from 1.5 to 3.5 μ by 0.2 to 0.5 μ.

Staining.—This bacillus belongs to a group of organisms known as "acid fast," on account of their ability to resist decolorization by acids. The tubercle bacillus is very difficult to stain, and special methods have to be employed. The Ziehl-Neelson being the most satisfactory. This resistance to staining is probably due to a surrounding capsule that consists of a fatty or waxy substance, inasmuch as it can be colored by the fat stains, such as Sudan III. Under some conditions this bacillus may not possess its acid-fast properties, yet when inoculated into animals the same organisms will produce tuberculosis, and acid-fast bacteria will be found.

Cultures.—This bacillus only grows in artificial cultures, provided that the medium contains serum, glycerin, yolk of egg, or fragments of tissue. It is an aërobic organism and grows only at temperatures above 30° C. In the case of human tubercle bacilli growth ceases at 41° C., and in the case of the bovine-bacilli, at 44° to 45° C. The optimum temperature is 38° C. In order to obtain a pure growth it is best to first inoculate a guinea-pig with the suspected material. In the course of a couple of weeks the lymph-nodes will be enlarged, due to the disease. These should be removed with

aseptic precautions, portions carefully taken, and culture-tubes be inoculated. Many tubes should be used, as some will either show no growth or else may be contaminated.

After inoculating *blood-serum* the growth will be apparent to the naked eye after about twelve days in the form of small, white, round, scaly, dry looking colonies scattered over the surface of the medium. On further incubation the colonies become raised, but maintain their scaly appearance, and the margins are irregular in outline. This medium is not very satisfactory and is not much used.

Glycerin-agar, except for primary cultures, is the best medium upon which to grow the bacillus, particularly if a little glucose be added. The growth begins as on serum, but the colonies are both larger and more numerous. They rapidly become confluent, and form a thick, whitish, dry, rough, scaly layer. After being subcultivated a few times the growth becomes very abundant, moist, and greasy. When old the growth has a reddish tint. On *bouillon* containing glycerin and glucose the growth takes place in the form of a pellicle, which is dense, creamy white, dry, and very friable. The fluid remains clear, although the pellicle may eventually break in pieces and fall to the bottom of the tube. The organism will grow also on *glycerinized potato* and on Dorsett's *egg-medium*. This latter consists of the whites and yolks of eggs mixed, coagulated, and sterilized by the intermittent method. *Gelatin* cannot be used, as it melts at the temperature (37° to 38° C.) required for growth. During incubation the tubes should be closed, so as to prevent evaporation.

Bacillus lepræ is non-motile, non-flagellate, non-sporogenous, chromogenic, non-liquefying, non-aërogenic, aërobic, and acid resisting. It very closely resembles the tubercle bacillus in size and shape. It stains in very much the same way as the tubercle bacillus, but is not so resistant. Ordinary methods can be employed. It is more easily decolorized, however, by acids. With Gram's method it stains well.

Pathogenesis.—This is the organism that produces leprosy in man and monkeys; possibly in some of the lower forms of animals as well. The bacilli are found throughout the tissue

lesions, and have been recovered from the blood of leprous individuals.

Cultures.—For many years attempts to grow this organism were unsuccessful, but recently bacteria believed to be the true bacilli of leprosy have been grown on artificial media. This is doubted by some investigators. The organisms obtained are acid fast, and in many respects resemble those found in the tissues. Others, however, may be classed among the diphtheroid, on account of their similarity to the Bacillus diphtheriæ.

According to Duval, the most successful method is as follows: Egg-albumen or human blood-serum is poured into sterile Petri dishes and dried for three hours at 70° C. The excised leprous nodule is then cut into thin slices, which are distributed over the surface of the coagulated albumen. By means of a pipet the medium is bathed in a 1 per cent. sterile solution of trypsin. The Petri dishes are now placed in a moist chamber and incubated for a week or ten days. The bits of tissue soften to a thick, creamy consistence and the bacilli multiply enormously. They may then be transferred to serum-glycerin-agar or to ordinary agar plus 1 per cent. of tryptophan. The colonies on these media are moist and orange colored.

Culture.—Ordinary media. In gelatin punctures gas-bubbles quite frequently appear, but there is no liquefaction of the medium. Gives the so-called "nail growth." Will grow from 16° to 40° C.

B. diphtheriæ is a non-motile, non-liquefying, aërobic organism from 0.4 to 1.0 μ broad, by 1.5 to 3.5 μ long, slightly curved and with clubbed ends. Is found in the pseudomembranes of those suffering from diphtheria. It is peculiar in that in a pure culture there will be found individuals differing greatly in size and shape. These probably represent involution forms, as they are found in greatest numbers in old cultures.

Stain.—Ordinary methods, but particularly Loeffler's methylene-blue. Stains by Gram's. The ends take the stain more deeply than the middle.

Culture.—Ordinary media. Is obtained very easily in pure culture. The best medium is Loeffler's blood-serum mixture. On it there appears a smooth, smeary, yellowish-white layer

FIG. 85.—BACILLUS OF TETANUS WITH SPORES (Fränkel and Pfeiffer).

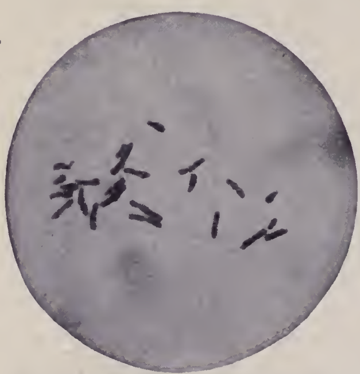


FIG. 86.—BACILLUS DIPHTHERIÆ, FIVE HOURS AT 36° C.

This shows only solid staining forms.

FIG. 87.—BACILLUS DIPHTHERIÆ, SAME CULTURE, EIGHT HOURS AT 36° C.

This also shows solid forms, many of them with parallel arrangement.

at the end of about twelve hours when grown at a temperature of 37° C. To make the diagnosis a swab of absorbent cotton is brought in contact with the suspected surface and the tube is then inoculated directly. A diagnosis can be made at the end of five hours. On gelatin the colonies appear as white points. On bouillon a distinct whitish pellicle forms on the surface. Also on agar, milk, and potato.

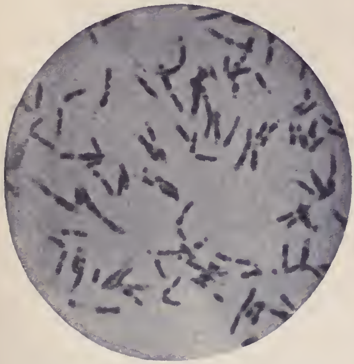


FIG. 88.—BACILLUS DIPHTHERIÆ, SAME CULTURE, TWELVE HOURS AT 36° C.

The bacilli stain faintly at their ends, and in some small granules are seen at the tip of the faintly stained portions.

FIG. 89.—BACILLUS DIPHTHERIÆ, SAME CULTURE, FIFTEEN HOURS AT 36° C.

The bacilli stain more unevenly and the granules are larger.

(Photomicrographs by Mr. Louis Brown. The magnification is the same in all— × 2000. All of the preparations were made from growth on blood-serum.) (Francis P. Denny, in "Jour. of Med. Research.")

Pathogenesis.—When introduced into the individual it causes on mucous membranes the formation of a pseudomembrane, composed chiefly of fibrin but containing desquamated epithelium and B. diphtheriæ. Is generally associated with both staphylococci and streptococci, giving rise to a mixed infection. Besides the local lesion there is a marked and serious intoxication, resulting from the absorption of poisonous metabolic products.

Preparation of the Diphtheria Antitoxin.—Virulent diphtheria bacilli are grown in alkaline bouillon containing 2 per cent. peptone for a period of three or four weeks at a temperature of 37° C. The culture is then heated for two hours at 65° C. and passed through a Chamberland filter. In this fluid there is the *toxin*. It is kept in sterile bottles in the dark.

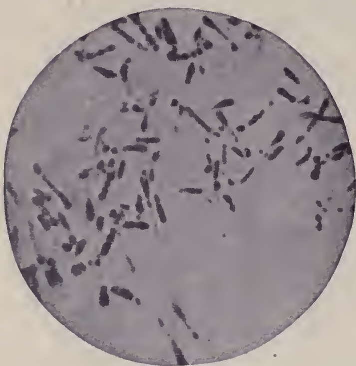


FIG. 90.—BACILLUS DIPHTHERIÆ, SAME CULTURE AS FIGS. 87-90, TWENTY-FOUR HOURS AT 36° C.

This shows clubbed and barred forms as well as granular forms. At the lower part of the field is a paired form which shows the characteristic clubbing of the distal ends.

FIG. 91.—BACILLUS DIPHTHERIÆ, FORTY-EIGHT HOURS AT 36° C.

This is the same bacillus as in Figs. 86–90, but from a culture where the colonies were discrete. It shows long filamentous forms.

(Photomicrographs by Mr. Louis Brown. The magnification is the same in all—× 2000. All of the preparations were made from growth on blood-serum.) (Francis P. Denny, in "Jour. of Med. Research.")

For the purpose of immunization the horse is the best animal, as it furnishes a greater amount of antitoxic serum in less time than when a smaller animal is used. The horse is injected hypodermically with 0.1 c.c. of the toxic filtrate. In the course of six days a larger dose is given; this is repeated

about every six days till from 500 to 1000 c.c. can be given without ill effects. When the degree of immunity is high the blood is withdrawn from a vein and collected in sterile bottles. These are placed on ice for about four days and the clear serum is drawn off from the coagulated blood. This serum is the *antitoxin*. It is preserved by the addition of 1:1000 formaldehyde, phenol, trikresol, etc.

The strength of the serum is designated by the term "immunizing units." According to Ehrlich and Behring, the "normal serum" is so strong that 0.1 c.c. of it would protect against ten times the least surely fatal dose of toxin when simultaneously injected into a guinea-pig. At present the "immunizing unit" is considered as containing ten times the least amount of antitoxin that will protect a 300-gram guinea-pig against the action of ten times the minimum fatal dose of the toxin.

To determine the strength of any given serum the minimum fatal dose of a sterile toxin for a 300-gram guinea-pig must be ascertained. Then determine the least quantity of the antitoxic serum that will protect a guinea-pig against ten times the minimum fatal dose of the toxin. The necessary dose of antitoxic serum is expressed as a fraction of a cubic centimeter and multiplied by ten, the result equaling one unit.

The value of the antitoxin depends upon its use in the early stages, before the third day. At the outset 4000 units should be given. In later stages 8000 to 10,000 should be given every four or six hours until the characteristic effect is produced. Except in very young children, the age should not affect the dosage. Smaller doses may be used as a prophylactic in those who have been exposed to diphtheria.

In severe cases more than one injection may be necessary. Amelioration of the local and general symptoms indicates the favorable action of the serum.

B. anthracis is a non-motile, sporogenous, liquefying, aërobic bacillus, from 1 μ to 1.5 μ in breadth by 5 to 20 μ in length. Has square ends and is found either singly or in long threads. The organism is found in the blood of the infected animal as well as in the local lesions.

Stains by usual methods and by Gram's.

Culture.—Grows readily on all media. On gelatin surface colonies appear as small, round, grayish-white dots, accompanied by liquefaction. In gelatin stabs there is a characteristic tree-like growth.

Grows at temperatures from 12° to 45° C. Toward the higher point there is marked formation of spores which appear as oval, transparent bodies situated at the middle of the bacillus and not causing any alteration in its shape.

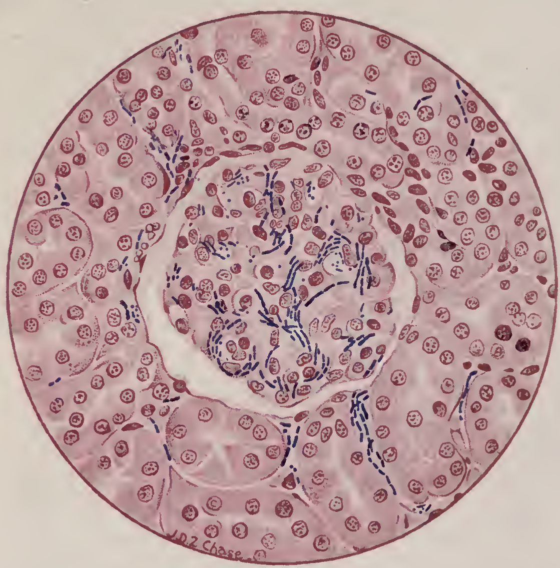


Fig. 92.—Anthrax Bacilli in Glomeruli of Kidney (McFarland).

Pathogenesis.—Is the cause of anthrax, wool-sorter's disease, or malignant pustule. It gains entrance by means of wounds, through the respiratory or through the alimentary tract. The viscera show marked congestion. Under the microscope numerous bacilli are seen in the capillaries.

Symptomatic anthrax is a motile, flagellated, sporogenous, anaërobic, liquefying bacillus about 0.5 μ in breadth and

3 to 5 μ in length, with rounded ends, found in the lesions of symptomatic anthrax.

Stains.—Usual ones. Not by Gram's.

Culture.—Is strictly anaërobic. Liquefies gelatin, and in stabs forms gas. Colonies are spherical or slightly irregular in outline. Forms large oval spores that distort the organisms.

Bacillus œdematis maligni is a motile, flagellated, anaërobic, liquefying, sporogenous bacillus, 0.8 to 1.0 μ in breadth

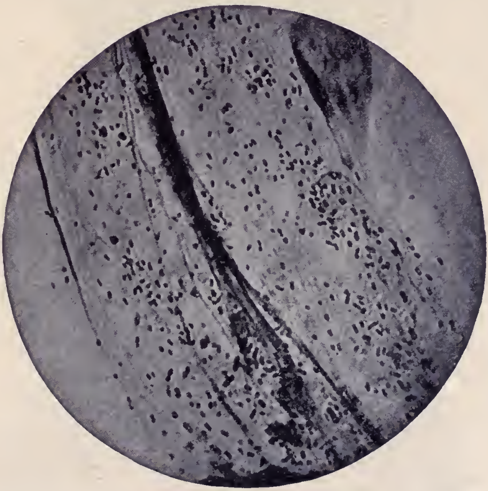


FIG. 93.—BACILLUS OF INFLUENZA. SMEAR FROM SPUTUM (after Heim).

and 2 to 10 μ in length, with rounded ends. Is found in garden earth, in the intestines of healthy animals, and in the lesions of the disease. Is not found in the blood on account of the oxygen present. May occur in long chains.

Stains.—Usual methods, but not Gram's.

Culture.—Ordinary media. On gelatin forms small, shining, grayish-white colonies. Under microscope can see long tangled filaments. In glucose-gelatin stabs forms white cloudy areas with some slight gas production.

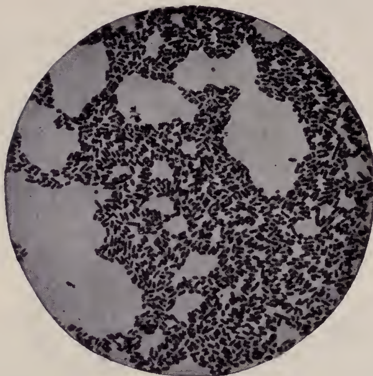


FIG. 94.—BACILLUS TYPHOSUS, FROM A TWENTY-FOUR-HOUR-OLD AGAR-AGAR CULTURE. × 650 (Heim).

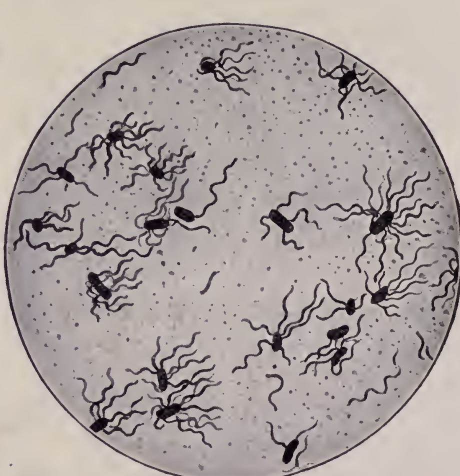


FIG. 95.—BACILLUS TYPHOSUS, SHOWING FLAGELLA (McFarland).

It is the cause of malignant edema. Is pathogenic for most animals, but cattle seem immune.

Bacillus influenzæ is a minute, non-motile, non-liquefying, aërobic bacillus found in the discharge from the nose and bronchi of those affected by influenza. Is also sometimes found in the blood. Is very small, about $0.2 \times 0.5\ \mu$, are usually single, but may occur in chains of three or four.

Stains.—Ordinary methods, but not by Gram's.

Culture.—Grows poorly on artificial media. Will not grow at all on ordinary gelatin or agar-agar. Develops best

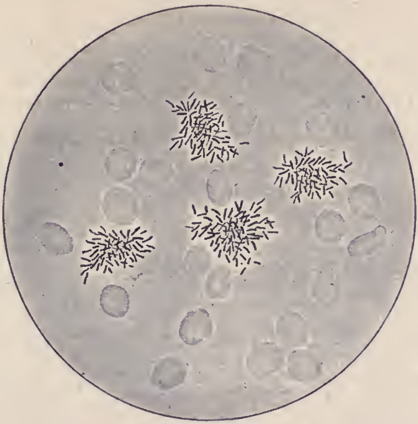


FIG. 96.—AGGLUTINATION OF THE TYPHOID BACILLUS BY A SPECIFIC SERUM.

upon media containing blood. Colonies appear as minute colorless bodies, looking like dewdrops. They do not coalesce. Is easily destroyed; 60° C. for five minutes will kill it. Will not grow below 28° C.

Bacillus typhosus is a motile, flagellated, non-sporogenous, non-liquefying aërobic, facultative anaërobic bacillus, 0.5 to $0.8\ \mu$ broad by 1 to $3\ \mu$ long, with rounded ends. Seldom seen in chains. Is found in the urine and feces of infected individuals; also in the blood, gall-bladder, and internal organs. Is present in water and milk as a result of contamination.

Stains.—Ordinary methods, but not by Gram's.

Culture.—Ordinary media. On potato there is formed a characteristic, thick, moist and shiny, invisible film.

Must be distinguished from the B. coli communis.

The following are the chief differences between the two:

	B. TYPHOSUS	B. COLI COMMUNIS
Colonies on gelatin plates:	On surface large, thin, and bluish, with notched border; yellowish brown in center. Deep colonies, brownish yellow and sharply circumscribed. Non-liquefying. Develop more slowly.	On surface large, yellow-brown, round or oval, with irregular border. Deep colonies, round, yellowish brown, homogeneous. Non-liquefying.
On potato:	Usually forms a thick, moist, and shiny invisible film. Sometimes yellowish or brownish.	Luxuriant growth. Yellowish brown and glistening.
Milk:	Slightly acidulated, but not coagulated. Diffuse cloudiness.	Rapid coagulating and marked acidulation. Turns blue litmus milk red, colors entire medium. Marked turbidity.
Peptone media:	No indol formation.	Indol formed within twenty-four to forty-eight hours.
Ferments:	No gas formed in media containing sugar.	Fermentation whenever sugar is present.
Potassium nitrate:	Not reduced.	Reduced to nitrites and then to ammonia.
Conradi-Drigalski medium:	Blue, transparent colonies.	Red, opaque colonies.
Endo agar:	Colorless colonies.	Red colonies.
Neutral red:	Color remains red.	Changed to yellow.
Agglutination test, Widal reaction:	Typhoid bacilli are clumped when acted upon by diluted serum from the blood of typhoid patients.	No clumping.

B. coli communis.—See typhoid. Structurally it resembles the B. typhosus.

B. pestis.—A minute non-flagellated, non-motile, non-sporogenous, non-liquefying aërobic bacillus. Is very short, $1.7\ \mu$ by $2\ \mu$, with rounded ends. Varies greatly in shape. Is found in the blood and in the enlarged lymphatic nodes.

Stains.—Ordinary methods, but not by Gram's. The rounded ends stain more deeply than the middle, giving an appearance of a diplococcus.

Culture.—Grows well on artificial media. Diffuse cloudiness in bouillon. Gelatin puncture growth scanty. On agar-agar forms white or bluish-white colonies with round, uneven edges. On agar-agar plus 2.5 per cent. salt forms marked involution forms. Best medium for culture is a 2 per cent. alkaline peptone solution containing 1 or 2 per cent. of gelatin.

Is the cause of bubonic plague in man. Is spread by means of rats and fleas.

Bacillus aërogenes capsulatus.—A large non-motile, non-flagellate, sporogenous, purely anaërobic bacillus, 0.5 μ broad by 3 to 5 μ long, and with rounded or square ends. Occurs in groups and in pairs, but not in chains, in this way differing from the anthrax bacillus. Is found in the tissues in the necrotic areas.

Stains.—Ordinary methods and by Gram's. The organisms obtained from the body show distinct capsules.

Culture.—Ordinary media, but in glucose gelatin shows best the characteristic gas-production. Is no distinct liquefaction, but the gelatin becomes softer. In deep stabs forms small, knot-like, grayish-white colonies from which extend fine hair-like or feathery projections. Produces acid.

Causes emphysematous gangrene with necrosis of the tissue before death and the formation of gas post-mortem.

Spirillum choleræ asiaticæ is a motile, flagellated, non-sporogenous, liquefying aërobic, and facultative anaërobic spirillum; found in short arcs, spirals, and "comma" forms. About 0.8 μ long. Has a single end flagellum. Is found in the feces, never in the blood or tissues, of those suffering from Asiatic cholera.

Stains.—Usual methods, but not by Gram's.

Culture.—Easily cultivated. On gelatin plates colonies appear in lower layer as small white dots. Extend to surface, causing liquefaction. Are granular. Gelatin stab cultures show liquefaction gradually extending from the surface

downward. Gives rise to an inverted cone with an air-bubble at the upper end. In liquid media the presence of indol and of nitrites is shown by the addition of one or two drops of chemically pure sulphuric acid, a reddish color being produced. Forms acid, but does not coagulate milk.

The spirilla resembling that of cholera are the following:

Finkler-Prior spirillum.—Similar in shape, but shorter and stouter. Actively motile. Growth rapid. Does not

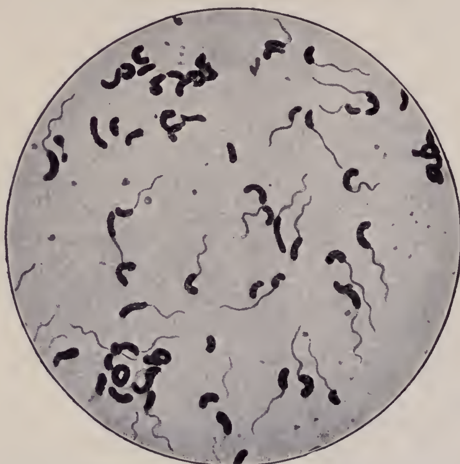


FIG. 97.—CHOLERA SPIRILLA, SHOWING FLAGELLA (Muir and Ritchie).

produce indol. Causes extensive liquefaction of gelatin. Is found in the feces of cholera morbus.

Vibrio tyrogenum.—Found in old cheese. Similar in form. Growth and liquefaction faster than S. cholera, but less rapid than Finkler. Is actively motile and has an end flagellum. Forms yellow, irregular, distinctly circumscribed colonies.

Vibrio Metschnikovi is a spirillum closely resembling that of cholera and is found in the feces of chicken cholera. Is somewhat thicker and shorter than the S. choleræ. Growth is very similar to that of the cholera spirillum, but is slower. Not pathogenic for man, but kills chickens, pigeons, and guinea-pigs.

Spirillum of relapsing fever is a long, undulating, actively motile, flagellated spirillum, about 0.1 μ in diameter and 20 to 40 μ long. Non-sporogenous. Are found in the blood of patients during the height of the attack, but disappear after the temperature has fallen.

Stains by ordinary methods, but not by Gram's.

Culture.—Has never been grown outside of the body.

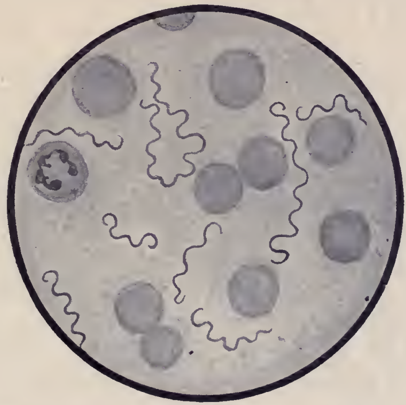


FIG. 98.—SPIRILLA OF RELAPSING FEVER IN HUMAN BLOOD. × 1000 (Boston).

Can be transmitted to monkeys by inoculating with infected blood.

Treponema pallidum (*Spirochæta pallida*) is an organism that is generally conceded to be the cause of syphilis. It has been found, by observers in all parts of the world, in the lesions of the primary and secondary stages; it is constantly present in the lesions of congenital syphilis; it is found in the blood of persons suffering from syphilis; and it is never found either in healthy individuals or in persons suffering from diseases other than syphilis. This organism is very delicate, actively motile, non-refracting, is long, thin, spiral or corkscrew shaped, with pointed ends. When stained they measure from 6 to 15 μ long by 0.25 μ across. Occasionally much longer forms are encoun-

tered, but these consist of several parasites attached to each other end to end. They show from six to fourteen turns, which are short, clear cut, and regular. Extremely delicate flagellæ have been demonstrated at the ends. No undulating membrane has been seen.

This organism stains with difficulty and, as a rule, very lightly; consequently, special methods have to be employed. In smears the best results are obtained with Giemsa's or Romanowsky's solutions. In tissues, Levaditi's method of nitrate of

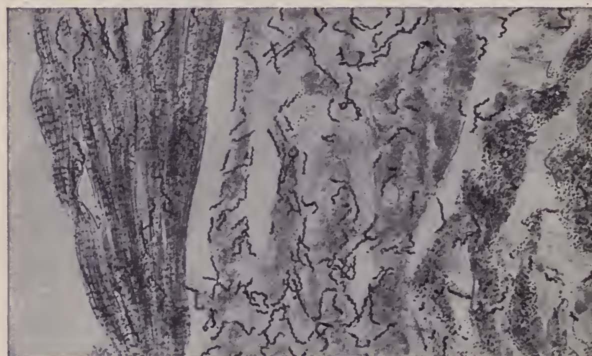


FIG. 99.—SYPHILIS, CONGENITAL. HEART (Mallory). Treponemata pallida in connective tissue and between muscle-fibers.

silver and pyrogallic acid gives beautiful results in formalin-fixed specimens, the treponemas staining black; the tissues, yellow. The most rapid and perhaps the most reliable method for finding the treponema is the examination with dark-ground illumination. Special apparatus is needed for this. The treponemas will stand out brightly against the black background of the preparation and are easily seen. Is Gram-negative.

Pathogenesis.—This organism is, without doubt, the cause of syphilis. As stated above, it has been found in the various lesions of the disease, and, now that it can be cultivated, Koch's postulates can be fulfilled. The disease has been reproduced experimentally in the higher forms of apes.

Cultures.—Until recently the treponema could not be cultivated artificially, but Noguchi has succeeded by using special methods. By inoculating syphilitic material into the testicles of rabbits he was able to get rid of contaminating organisms. Portions of this tissue are later transferred to a medium that consists of 1 part serum with 3 parts distilled water. The tubes are then incubated under anaërobic conditions. The treponemas begin to multiply after about forty-eight hours, and continue to increase slowly for four to five weeks. They attain their natural size in ten to twelve days, and later elongate and form tangled masses.

Diagnosis.—The method devised by Wassermann of applying the complement fixation-test has been used very successfully in diagnosing this condition. It has been determined that if a hemolytic system be added to a mixture of extract of syphilitic liver, heated syphilitic serum, and complement, no hemolysis occurs. The method is described fully under the heading of Wassermann Reactions (see p. 185).

Spirochæta refringens.—This organism is very commonly associated with the Treponema pallida in the syphilitic lesions, but can be distinguished readily. It is larger and longer, and in the fresh condition is highly refractile. The turns of the spiral are fewer, longer, less regular, and flattened. The impression given is that of a piece of ribbon. Its movements are more rapid than those of the Treponema pallida, and it stains easily with the ordinary dyes, and colors blue with Giemsa's solution instead of red or pink.

Spirochæta balanitidis has been found in cases of ulcerative balanitis, and would appear to be identical with the S. refringens.

Spirochæta plicatilis is a large, thick spirochete which stains easily. The curves are widely separated and large, and an undulatory membrane is present.

Spirochæta dentium.—This spirochete multiplies in carious teeth, and more closely resembles the Treponema pallidum than any other species. In common with the treponema it is an organism of very delicate structure, only slightly refractile in the fresh condition, and the turns of the spiral are regular and

permanent. It is, however, shorter than the treponema, its average length being 4 to 10 μ, and the turns of the spiral are closer together and not so deep. It also stains more easily than the organism of syphilis. According to Noguchi, there are at least two varieties: the *S. microdentium* and the *S. macrodentium*, the former being the one that resembles the syphilitic organism. In making smears for staining or for dark-field illumination, when the lesions are in the mouth, great care must be observed in order to prevent mistakes in diagnosis.

Spirochæta buccalis is a large organism with few undulations. Stains easily, and should give no difficulty in distinguishing between it and the Treponema pallidum.

Spirochæta vincenti.—This spirochete, found in association with the fusiform spirilla, has the same characters as the S. buccalis. It must be regarded as either very closely related to, or identical with, that organism.

Treponema pallidulum (*Spirochæta pertenuis*) is an organism very closely related to that of syphilis. It is the cause of frambesia, or yaws, a contagious and inoculable disease very common in the tropics, and characterized by papillomatous lesions that do not involve the mucous membranes.

Bacillus fusiformis is a long, rod-shaped organism measuring 5 to 10 by 0.6 to 0.8 μ, slightly swollen in the middle, and pointed at the ends. It stains readily with the ordinary dyes. The majority of observers state that it is Gram-negative, but others believe it to be Gram-positive. It is nearly always associated with the *Spirochæta vincenti*.

Pathogenesis.—This organism was described originally as occurring in cases of hospital gangrene. It is more common at present in the form of Vincent's angina (see p. 380), an inflammatory condition of the throat.

Cultures.—It has been obtained in pure culture by growing upon the surface of ascitic fluid agar under strictly anaërobic conditions at 37° C. After two or three days the fusiform bacilli appear in the form of delicately whitish colonies, resembling colonies of streptococci. It has also been grown on rabbit's blood agar, and on Löffler's blood-serum. From all of the cultures a somewhat offensive odor is given off.

CHAPTER XIV

PARASITES

A *parasite* is an organism that lives in or upon another. Many are harmless, but some of them are distinctly pathogenic, as they live at the expense of the individual, to the detriment of its well-being.

The body at whose expense the parasite lives is called the *host*.

Parasites may be divided into the *vegetable* and the *animal* varieties. Those living within the body are known as *endoparasites*, those upon the surface of the body, as *ectoparasites*.

Parasitic diseases are characterized by having a specific exciting cause, and by the fact that they can be transferred from one individual to another. Some forms go through a portion only of their life history as parasites.

Others are able to live without the host, and are known as *optional* or *occasional* parasites. To this class belong many of the insects, as mosquitoes.

Some cannot live independently and are known as *obligatory* parasites, such as the tapeworms. They have no sense-organs, alimentary tract, or circulation. They have no need of such structures, as their food is taken up by absorption. The organs by which they retain their grasp and their powers of reproduction are well developed.

Pathologic conditions due to parasites may be the result of *mechanical* or *chemical* phenomena.

Mechanical, as obstruction of the lumen of an intestine, vessel, or duct; hemorrhage resulting from bites and suction, pressure.

Chemical: disturbances resulting from the absorption by the host of poisons, or from degenerative processes, causing reflex nervous symptoms, inflammation, and irritation.

ANIMAL PARASITES

Protozoa.

Entamœba coli.
Entamœba histolytica.
Coccidium oviforme.
Trichomonas intestinalis.
Cercomonas intestinalis.
Trichomonas vaginalis.
Plasmodium malariæ.
Yellow fever.
Trypanosomes.
Pyrosoma.

Vermes.

Cestodes. Tapeworms.

Tænia solium.
Tænia saginata.
Dibothriocephalus latus.
Tænia echinococcus.
Hymenolepis nana.
Tænia cucumerina.

Trematodes. Sucking worms.

Fasciola hepaticum.
Dicrocœlium lanceolatum.
Schistosoma hæmatobium.
Parogonimus westermanni.

Nematodes. Round-worms.

Ascaris lumbricoides.
Oxyuris vermicularis.
Eustrongylus gigas.
Filaria medinensis.
Filaria bancrofti.
Uncinaria duodenale.
Necator americana.
Strongyloides stercoralis.
Trichinella spiralis.
Trichuris trichiura.

PROTOZOA

Definition.—The protozoa are with few exceptions, unicellular organisms of a primitive type, reproducing by division, by budding, and by spore formation. They consist of protoplasm which is differentiated into cytoplasm and nucleus, both of which may show many variations throughout the more or less complicated life cycle that each individual undergoes. Some

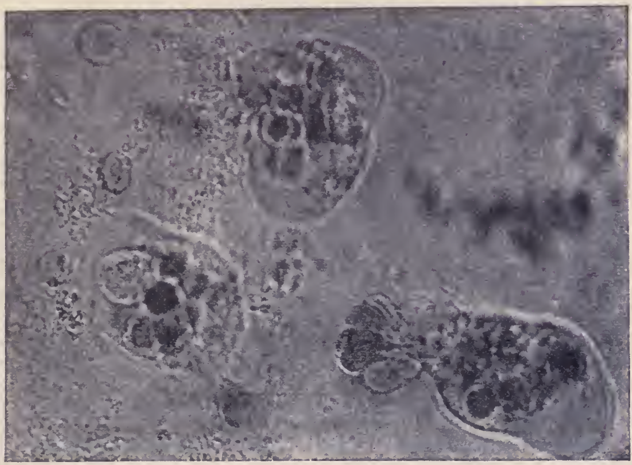


FIG. 100.—ENTAMŒBA HISTOLYTICA. LIVING ORGANISMS. NOTE ABSENCE OF NUCLEUS. ALL THREE OF THE PARASITES CONTAIN RED BLOOD CORPUSCLES. × 750. (Bulletin No. 1, Medical Department, U. S. Army).

protozoa maintain an independent existence, others are parasitic for men and lower animals.

Transmission may occur by *contact*, by *ingestion* with food or drink, or it may be by means of *intermediate hosts*. This is the case in malaria, yellow fever and with some of the trypanosomes. The more common carriers are mosquitoes, flies, ticks, bed-bugs and leeches.

The following are the more important members.

Entamœba Histolytica.—Vary in size from 25 to 35 μ in diam-

eter. Have a distinct, dense, hyaline covering. The pseudopods are large, finger-shaped refractile, and few in number. The granular cytoplasm contains bacteria, starch granules, and red and white blood-cells in various stages of disintegration. Vacuoles may be present. This protozoan is now conceded to be the cause of the acute and chronic dysenteries that occur in tropical and semi-tropical regions.

It is able to penetrate the mucous coat of the intestine and undergo multiplication in the submucosa. The blood-supply is shut off and the tissue breaks down, giving rise to the characteristic undermined ulcers of tropical dysentery.

The intestine is its usual habitat, but it may be found in solitary abscess of the liver that so commonly follows dysentery.

The E. tetragena is probably identical with the E. histolytica. The *E. coli* is very frequently found in the intestine under normal conditions but is probably non-pathogenic.

Coccidium oviforme is an elliptical parasite that is rarely found in the intestines and liver of man, but is common in rodents. It has a distinct double capsule, is found within cells in which it undergoes rapid division. Frequently becomes encysted, and when taken into the intestine, the capsule is dissolved and the organism is set free.

Other less important parasites are the **Paramœcium coli,** an ovoid, unicellular organism about 7 to 10 μ long. Is surrounded by short cilia. Usually contains numerous large vacuoles. Is found in diarrheal feces.

The **Trichomonas intestinalis** is a pear-shaped organism about 10 to 15 μ long. On one side it has an undulating membrane provided with about 10 to 12 cilia. Is found in intestinal discharges in diarrhea, typhoid fever, and cholera.

The **Cercomonas intestinalis** is a pear-shaped parasite about 10 to 12 μ long. From its blunt end extends a single flagellum.

The **Trichomonas vaginalis** is an oval organism about 10 μ long. To one end are attached three long flagella, near the base of which is an undulating membrane provided with five to six cilia.

PLATE I.

PLATE I.

Various Forms of Malarial Parasites (Thayer and Hewetson).

Figs. 1 to 10, inclusive, tertian organisms; Figs. 11 to 17, inclusive, quartan organisms; Figs. 18 to 27, inclusive, estivo-autumnal organisms.

Fig. 1.—Young hyaline form; 2, hyaline form with beginning pigmentation; 3, pigmented form; 4, full-grown pigmented form; 5, 6, 7, 8, segmenting forms; 9, extracellular pigmented form; 10, flagellate form.

Fig. 11.—Young hyaline form; 12, 13, pigmented forms; 14, fully-developed pigmented form; 15, 16, segmenting forms; 17, flagellate form.

Figs. 18, 19, 20.—Ring-like and cross-like hyaline forms; 21, 22, pigmented forms; 23, 24, segmenting forms; 25, 26, 27, crescents.

It has been found in the urine as well as in the vagina.

The **Hæmameba malariæ** is a unicellular protozoan parasite that, during one cycle of its existence, lives in the blood and brings about a destruction of the erythrocytes. Its other cycle is carried on within the body of a mosquito, the Anopheles.

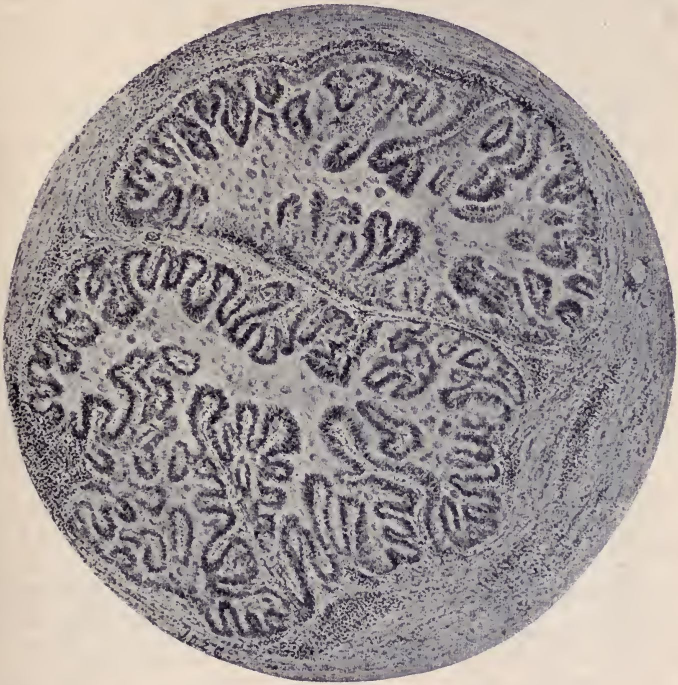


FIG. 101.—COCCIDIOSIS OF RABBIT'S LIVER (McFarland).
Section of one of the affected bile-ducts, showing the papillary outgrowths from the mucous membrane and the signs of inflammation in the surrounding tissue.

There are three varieties of the organism:

1. The *quartan* parasite, *Hæmameba malariæ*, attains its development in three days. It appears inside an erythrocyte as a small, unpigmented, irregular, hyaline body capable of slow ameboid movement. It grows gradually, and brownish

or black granules appear within a few hours. The erythrocyte becomes gradually paler and is finally completely filled by the plasmodium.

The pigment occupies the center of the cell, and later the parasite splits up into from six to twelve pear-like segments which, along with the pigment, escape into the circulation. Is the rosette form. The granules in this form are larger and darker than in the tertian, but not so numerous.

Double infection may occur, in which case there would be paroxysms for two days, then an intervening free day.

2. The *tertian* parasite, *Hæmameba vivax*, requires two days for its development. In its early stages it resembles the quartan parasite, but it eventually becomes larger. The tertian continues growing until it may be double the size of a red cell, usually but slightly larger. The pigment particles appear in about six hours, at first scattered, but finally collect in the center and are actively motile. The organism then divides into fifteen to twenty small, round, spore-like bodies, resembling a bunch of grapes. This form of parasite contains more granules than the quartan, but they are smaller and the red corpuscle is rapidly decolorized.

3. The *æstivo-autumnal* parasite, *Hæmameba falciparum*, is probably a tertian form. Is sometimes spoken of as malignant tertian.

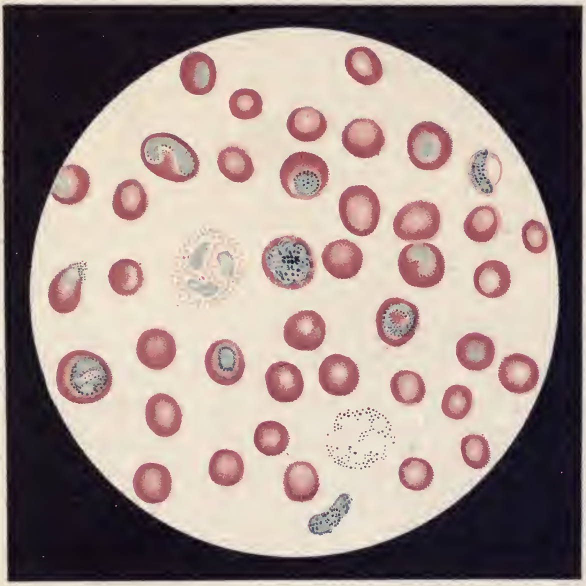
The cycle of development lasts forty-eight hours. The organism is smaller than in the first two, but more active. When fully developed, it is about one-third the size of the red cell.

When at rest, it assumes the signet-ring form—a disc with a colored outline. The pigment develops within twenty-four hours in the form of a few coarse granules centrally located; is non-motile.

The organism finally becomes lobulated, rosette-shaped with the pigment in the center or toward the periphery, and divides into six to twelve little balls.

The development of this form seldom takes place in the peripheral blood, usually in the spleen, bone-marrow, and cerebral capillaries.

PLATE II.



Malarial Parasites in Blood (Grawitz).
Numerous pigmented parasites, spore formation of the tertian type, and two crescents.

TABLE SHOWING CHIEF DIFFERENCES BETWEEN THE SPECIES OF MALARIAL ORGANISMS (GENUS HÆMAMEBA) FOUND IN MAN (Park and Williams).

Name of organism	Size of parasite up to segmentation (schizont)	Motion of young schizont in corpuscle	Time of appearance of melanin granules and their arrangement	Shape of segmenting parasite, number of segments, and site of segmentation	Asexual cycle complete in	Sexual forms	Incubation period	Effect on human host tissues	Remarks
H. vivax (parasite of tertian fever).	1 μ to slightly larger than normal red blood-cell (may occasionally be almost twice size).	Markedly active.	6 hours. First scattered, then gathered in center. Finely granular. Actively dancing.	Irregular mulberry. 12–24 (average 16). Peripheral circulation.	48 hours.	Gametocytes spherical. No crescents. Male ⅔ size of female, which is 1½ times size of red blood-cell. No crescents.	About 14 days.	Pale, granular, slightly enlarged red-blood-cells. Finely granular pigment formed from metamorphosed hemoglobin.	Double infection may cause a paroxysm every day, thus giving clinically a quotidian type of fever.
H. malariæ (parasite of quartan fever).	1 μ to little less than size of blood cell.	Not very active.	Within a few hours. Collected in zone on periphery. Coarsely granular. Slight dancing.	Regular daisy shape. 6–10 (average 8). Peripheral circulation.	72 hours.	Gametocytes spherical. Fewer than in vivax. About size of red blood-cell. No crescents.	About 3 weeks.	Red blood-cells may be slightly shrunken.	Double infection may cause a paroxysm every day, thus giving clinically a quotidian type of fever.
H. falciparum (parasite of estivo-autumnal (pernicious) fever type).	Smaller than others, from very small to ½ diameter corpuscle.	Active, but slightly less so than tertian type.	Within 24 hours. Small amount, 2–3 coarse granules usually central. Non-motile or sluggish.	More or less symmetrical daisy. 10–32 very small. Chiefly in bone marrow and viscera.	24–48 hours.	Gametocytes crescentic, short and plump. ¾ size of red cell.	About 10 days.	Red blood-cells unstained, greenish, shriveled (crenated) and darkened; stained (Giemsa) salmon color.	

The erythrocytes tend to shrivel and become dark. In this variety of infection are found the *crescents* of Laveran. They are oval or crescentic bodies that are pigmented in their center and have no ameboid motion, but are able to slowly alter their shape.

When fully developed are larger than a red cell. They are found partly in red corpuscles, or clinging to them, free in the blood and sometimes in leukocytes. Occur only in the severe forms of malaria; are probably malignant tertian parasites that have failed to sporulate.

When the organisms sporulate and are set free within the blood, the fever rises and the chill takes place. The escaped spores enter other red corpuscles, go through the same cycle, and a continuous reinfection occurs.

The foregoing cycle is the asexual one, *schizogony*, that takes place within the human body. It is now definitely settled that infection takes place by means of the bite of certain mosquitoes belonging to the genus Anopheles. Of mosquitoes, only the female bites.

This insect withdraws the malarial parasites from an infected individual; these undergo the sexual stage of development, *sporogony*, and are again transmitted to other people by the mosquito biting.

In the blood of an infected person two chief forms of parasite are found. One that is the smaller is round and contains numerous granules and is called the *microgametocyte*. From it flagella—*microgametes*—are given off. These flagella penetrate a larger spherical form that has a clear protoplasm, the *macrogamete*, which has formed from the *macrogametocyte* by the extrusion of small reduction nucleus; the former being the male, the latter the female, element. The impregnated parasite is called a *zygote*. These zygotes penetrate the stomach and become attached to the outer wall, where they grow much larger and are called *sporocysts*. They finally undergo division into secondary spheres, *sporoblasts*, which ultimately split up into very many small, spindle-like bodies known as *sporozoites*. These escape into the body cavity of the mosquito and the majority finally gain entrance

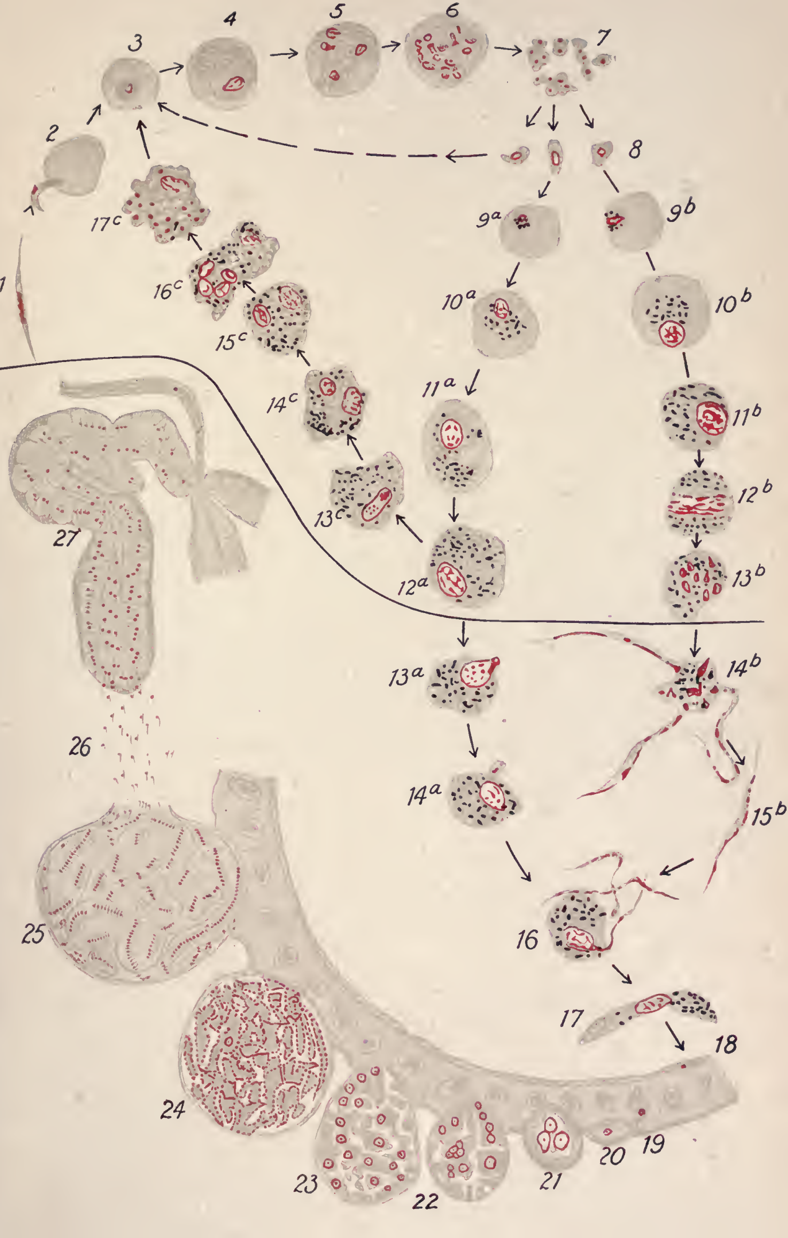
PLATE III.

LIFE-CYCLE OF PLASMODIUM VIVAX (after Grassi and Schaudinn)

The human cycle is above the transverse line, somewhat rearranged by Kisskalt and Hartmann. The cycle in the mosquito is beneath. 1 to 7, schizogony; 1, sporozoite; 2, entrance of the sporozoite; 3, 4, growth of the schizont; 5, 6, nuclear division of the schizont; 7, formation of the merozoites; 8, merozoites; 9*a* to 12*a*, growth of the macrogametocyte; 9*b* to 12*b*, growth of the microgametocyte; 13*c* to 17*c*, parthenogenesis of the macrogametocyte; 13*a*, 14*a*, maturation of the macrogamete; 13*b*, 14*b*, growth of the microgamete; 15*b*, microgamete; 16, fructification; 17, oökinet; 18 to 20, entrance of the oökinet into the stomach-wall of the mosquito; 20 to 25, sporogony; 22, 23, nuclear multiplication in the sporont; 24, 25, formation of the sporozoites; 26, passage of the sporozoites to the salivary gland; 27, salivary gland of the mosquito with sporozoites. (Magnification, 1 to 17*c*, 1200 to 1; 18 to 27*c*, 600 to 1.)

(Park and Williams' "Pathogenic Micro-organisms.")

PLATE III.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into the salivary glands, from which they escape in the secretions.

When the blasts gain entrance into the blood, they attack the red corpuscles and give rise to malaria.

In this case the mosquito is the definitive host of the parasite, man the intermediate.

The cycle of development in the mosquito varies according to the type of malarial organism—about three weeks in the quartan, two weeks in the tertian, and twelve days in the estivo-autumnal.

The following is a description of the Anopheles mosquito. Palpi in both sexes, nearly as long as the proboscis, 4 jointed in females, 3 in male. Is a constricted basal joint in each. Palpi are straight and parallel with proboscis except when female is biting, then they diverge.

Nucha has scaly posterior cornu, abdomen hairy on both surfaces, not scaly. Legs long and end in simple dentate claws. Wings spotted, and these spots when magnified are seen to be made up of black squamæ on brownish wing.

Length of female 7.5 to 9 mm., including proboscis; male smaller and does not bite.

When resting on a perpendicular wall the Anopheles extends its body at right angles unless it is filled with blood, the Culex holds its body parallel.

Yellow fever is an infectious disease, probably caused by some protozoön which is carried by a mosquito, the *Aedes* (*Stegymia*) *calopus*.

The female mosquito is from 3.5 to 5 mm. long, head clothed with flat scales, black and gray on each side. A white patch in the middle in front, extending back to the neck. A white patch on each side and thin white borders to the eyes. Antennæ blackish with narrow pale bands. Last joint of palpi white on inner side. Thorax dark brown, ornamented with white curved band on each side of the back and white spot on each side in front.

Abdomen dark with basal bands of white.

Fore- and mid-ungues toothed, hind ones not.

This mosquito may convey yellow fever to a non-immune

as early as on the twelfth day after biting an infected person, and it may retain the power to do so as long as it lives.

This disease can also be transmitted by the hypodermic injection of blood drawn from a patient in the first, second, or third days of the disease. It cannot be communicated by fomites.

The infected agent can be passed through a filter that is impermeable to ordinary bacteria and is destroyed by a temperature of 55° C. maintained for ten minutes.

One attack usually renders a person immune.

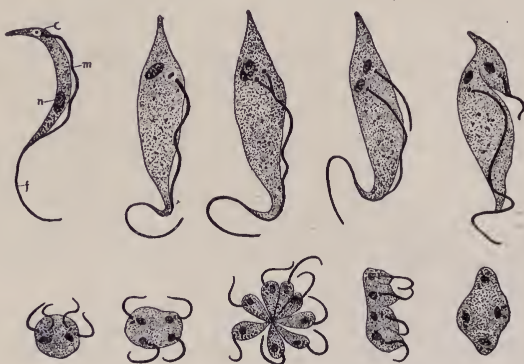

FIG. 102.—TRYPANOSOMA, SHOWING MULTIPLICATION BY DIVISION (from Laveran).

n, Nucleus; *c*, centrosome; *m*, undulating membrane; *f*, flagellum.

Trypanosomes.—Typical trypanosomes are characterized by a comparatively long, spirally twisted body, 8 to 35 μ, along one side of which is attached an undulating membrane having a cord-like edge that is continued forward as a flagellum. This flagellum arises near the posterior end of the organism in a small granule, called the *blepharoplast*, which lies near, or may be merged with, a large chromatin mass, called the *kinetonucleus*, because of its control over the motor apparatus. The nuclear apparatus consists of a *trophonucleus* with an intranuclear centrosome.

Multiplication takes place by longitudinal division. The

centrosome first divides, the posterior end then shows signs of cleavage; the undulating membrane is soon seen to double beyond the point of separation, and the division extends anteriorly until connected only by the flagellum, which soon separates.

Life cycle is not well known. Though transmission occurs through the bites of various invertebrates, notably flies, no definite sexual changes have been proved to take place in the intestines of these intermediate hosts. In one variety, "dourine," no intermediate host seems necessary, the infection occurring through coitus.

Many of these organisms have been artificially cultivated.

These bodies are found in the blood in certain diseases of man and the lower animals.

Tsetse-fly Disease.—"Nagana." In this infectious disease of lower animals the blood shows the presence of the *Tr. brucei.* It is transmitted to healthy animals by the bite of a fly—the *Glossina morsitans.*

Sleeping sickness or human trypanosomiasis is an infection by the *Tr. gambiense* which is conveyed by a fly—the *Glossina palpalis.* The organisms are present in the blood for a long time before entering the cerebro-spinal fluid and giving rise to the characteristic symptoms, increasing weakness, emaciation, lethargy, coma and death.

Piroplasmosis.—Is a group of severe and commonly fatal affections caused by peculiar minute protozoan parasites belonging to the genus Piroplasma.

Texas fever is an acute febrile disease of cattle resulting from the presence in the blood of the *Pyrosoma bigeminum.* Parasites are extremely minute, 2 to $4\mu \times 1.5$ to 2μ, are rounded at one end, pointed at the other, and associated individuals always have the points directed at one another. As a rule, are enclosed within the red corpuscles. In this disease the common cattle tick, *Rhipicephalus annulatis* (Boöphilus bovis), is the means by which it is spread. This parasite is peculiar in that it passes into the eggs of the tick and infects the embryos.

Montana spotted fever is a peculiar acute febrile disease found in a certain part of Montana, and supposed to be caused by a blood parasite resembling the pyrosoma of Texas fever. Is thought that it is transmitted by a woodtick, Dermacentor andersoni, that has first obtained blood from a variety of squirrel.

Leishmania donovani are peculiar parasites discovered in the splenic pulp in patients in India suffering from Dumdum fever. These bodies are extremely minute, ovoid organisms, enclosed singly or in groups in the splenic cells, or enclosed in amorphous masses of albuminous substance apart from the cells. They are each provided with a macronucleus, whose long diameter corresponds to that of the body itself, and a micronucleus, much smaller, more elongate and slender, placed perpendicularly to it. Similar bodies have been found in the spleen in tropical splenomegaly, known as "kala-azar," in "Delhi sore," and in patients in Panama.

Was at first thought that these organisms belonged either to the trypanosomes or to the piroplasma, but at present they are classed by themselves.

WORMS

Cestodes or **tapeworms** are more or less elongated, flattened, and segmented bodies that attach themselves to the mucous membrane of the intestine by means of suckers or hooklets.

They have no alimentary canal. Are hermaphroditic. One cycle of their life-history is in man, the other in some one of the lower animals. The fully developed worm is called a *strobile*. It consists of a head, a very narrow neck, and a number of segments called *proglottides*. These segments complete or the eggs from them escape in the feces. They are then taken up in the food, the covering of the egg digested, and the embryos penetrate the tissues, ultimately lodging in the voluntary muscles and elsewhere. The embryo worm when lodged in the tissues is called a *scolex*, consisting only of a head and vesicular body without a trace of organs, and is surrounded by a bladder-like body known as a *cysticercus*. When the animal

food is eaten, the embryos are set free, and attach themselves to the intestine.

Tænia solium, or pork tapeworm, is usually about 3 meters long, with from 800 to 900 segments. The head has a rostellum armed with a double row of from 26 to 30 hooklets and four suckers on the sides. The uterus consists of a median tube, with from 6 to 12 coarse lateral tubes. The genital pore is on alternate sides of the segments, which, when mature, are longer than they are broad.

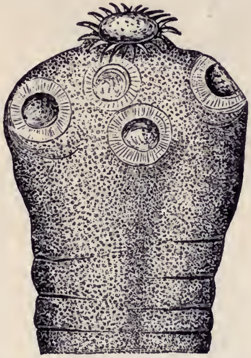

FIG. 103.—HEAD OF TÆNIA SOLIUM (Mosler and Peiper).

FIG. 104.—MATURE SEGMENTS OF TÆNIA SOLIUM (Mosler and Peiper).

FIG. 105.—EGGS OF TÆNIA SOLIUM (Mosler and Peiper).

The eggs are oval, about 30 to 35 μ in diameter, and consist of a peripheral striated zone and a central granular portion in which can be seen six lines representing hooklets. The embryos occur in pork as measles, and as Cysticercus cellulosæ

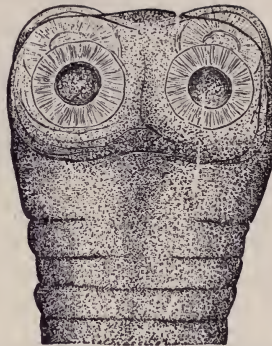

FIG. 107.—HEAD OF TÆNIA MEDIOCANELLATA (SAGINATA) (Mosler and Peiper).

FIG. 106.—TÆNIA SOLIUM (Mosler and Peiper).

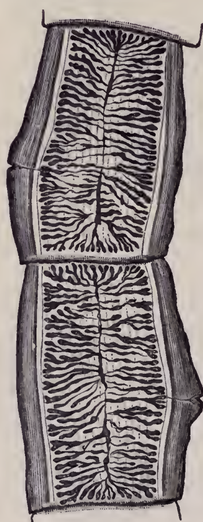

FIG. 108.—MATURE SEGMENTS OF TÆNIA MEDIOCANELLATA (SAGINATA) (Mosler and Peiper).

FIG. 109.—EGGS OF TÆNIA MEDIOCANELLATA (SAGINATA) (Mosler and Peiper).

in the muscles, brain, and eye of man. They gain entrance in uncooked pork.

Cysticercus cellulosæ is the larval stage of the T. solium. Is an elliptical, translucent, bladder-like structure, 6 to 12 mm. long by 5 to 10 mm. broad, with a white spot at its

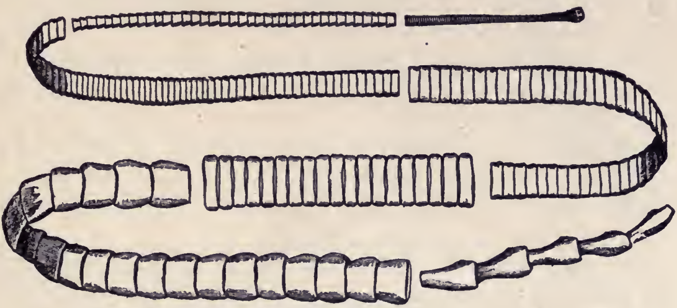

FIG. 110.—TÆNIA MEDIOCANELLATA (SAGINATA) (Eichhorst).

equator, due to the invaginated head. May be found in all parts of the body. Takes about six months for the embryo to develop to the bladder-worm stage.

The **Tænia mediocanellata (saginata)**, the beef tapeworm, is the most common variety. It varies in length from 4 to 8

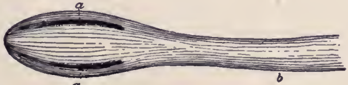

FIG. 111.—HEAD OF DIBOTHRIOCEPHALUS LATUS (Blanchard).
a, *a*, Bothridies; *b*, neck.

FIG. 112.—RIPE SEGMENTS OF DIBOTHRIOCEPHALUS LATUS (Mosler and Peiper).

meters, with about 1000 segments. Head is small, is flattened on the top, has no rostellum nor hooklets, but possesses four sucking discs.

The uterus is like that of T. solium, but possesses from 20 to 30 lateral branches which frequently divide dichotomously. The genital pore is on alternate sides of the proglottides, which are longer than they are broad when fully matured. The eggs are a little larger and more oval than those of T. solium, otherwise very similar. Results from the eating of improperly cooked beef.

The **Tænia echinococcus** in its adult form is found in the intestinal tract of the dog, the larval form occurring in man and some of the lower animals.

It is quite short, about 4 or 5 cm. long, and consists of four segments. The head, which forms the first, is long, has four suckers and a rostellum having from 28–50 hooklets arranged in a double row.

The fourth segment is the largest and constitutes about two-thirds of the entire worm. It alone possesses a uterus which consists of a median portion with a few lateral branches. It contains numerous long oval eggs with very thin shells. The eggs enter the intestine, the shells are dissolved and the embryos set free. They penetrate various tissues, particularly the liver, become encapsulated, and slowly develop into cysts whose walls are made up of two layers—the outer cuticular, formed from the connective tissue of the host, and the inner granulocellular layer.

In the course of some weeks small projections grow from the inner layer and project into the primary cyst. These buds have hooklets and suckers and are embryo parasites. This variety of cyst is the *Echinococcus scoleciparíens*.

In the *Echinococcus hydatidosus* or *E. endogenes*, daughter and even grand-daughter cysts develop inside the original cyst. They probably result from a cystic change in the buds already mentioned. Sometimes secondary cysts form on the outside of the wall, the *E. exogenes*.

The *echinococcus multilocularis* is the variety in which there are a great many small cysts surrounded by dense connective tissue. These cysts contain pigment and calcareous matter, but seldom scolices; are usually sterile.

These various forms of echinococcus cysts are filled with a

clear fluid of about 1009 to 1015 specific gravity; is neutral or alkaline, contains no albumin, but sodium chlorid is present and sometimes sugar.

A cyst may become very large or the fluid disappear by absorption and inspissation.

It may be harmless or dangerous according to its location. May undergo suppuration.

Is usually found in the liver, but may occur in lungs, kidneys, spleen, omentum, and in the brain.

Fig. 113.—Tænia Echinococcus; Enlarged (Mosler and Peiper).

The **Dibothriocephalus latus** has for its host some kind of fish, usually the pike. It is the largest of the tapeworms, measuring from 5 to 9 meters in length and having at times as many as 4000 segments. The growth after infection is very rapid.

The head is long, flattened, and has two groove-like suckers on its sides. The neck is thin, gradually increasing in diameter.

The proglottides are broader than long and the uterus,

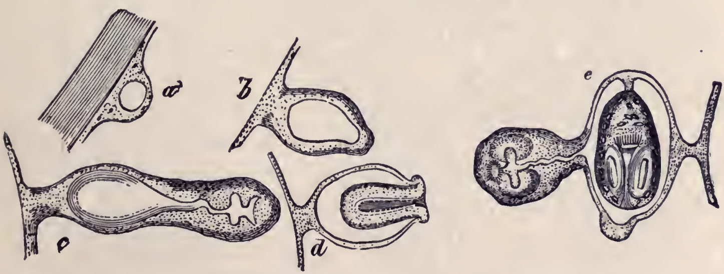

Fig. 114.—Development of Ovum. × 90 (Leuckart).
a, Suspended heads; *b*, primary rudiment of head; *c*, further development; *d*, intussusception of head; *e*, later budding.

instead of being branched, consists of a tube coiled upon itself in the center.

The genital pore is on the flat side of the segment, and always on the same side of the worm.

The eggs are oval and possess a shell-like cover which has a hinged lid at one end. These eggs develop in fresh water into a freely moving, ciliated embryo that finally enters the digestive tract of the fish.

The **Hymenolepis nana,** or dwarf tapeworm, is from 2 to 4.5 cm. long. Its head is rounded, has four suckers and a rostellum that may be protruded or retracted, on which is a single circle of from 22 to 27 hooklets. Are about 200 segments, all of which are broader than long.

The intermediate host is not definitely known—is possibly the rat. Embryos can develop in the rat into adult forms without an intermediate host. May do so in man.

The adult form alone is found in man. It attaches itself to the intestine by sinking its head deep into the mucous membrane.

The **Tænia cucumerina** or *elliptica* is the common tapeworm of cats and dogs. Is about 15 to 30 cm. long and has a

Fig. 115.—Eggs of Dibothriocephalus Latus (Mosler and Peiper).

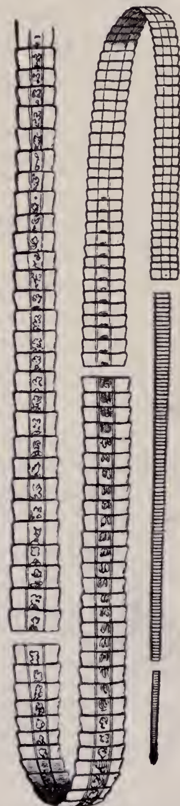

Fig. 116.—Dibothriocephalus Latus (Eichhorst).

head with a rostellum possessing 60 hooklets arranged in four rows. The rostellum can be protruded or retracted. The junction of the proglottides is much narrowed. Each segment has two genital pores, one on either side. The in-

termediary host is probably the dog louse or sometimes the flea.

Trematodes, or **sucking worms,** are flattened elliptic organisms that possess a sucking organ at the head end and another on the abdominal surface behind the short neck. They are usually hermaphroditic, but in some the two sexes occur.

The **Fasciola (Distoma) hepaticum,** or liver fluke, is from 15 to 35 mm. long and 6 to 20 in width. Is pointed bluntly at each end and has two suckers, one at the head, the other on the ventral surface. Between the two suckers is the genital pore. The eggs are oval, 0.14 mm. in length, and provided with a lid at one end. Is hermaphroditic, the genital pore acting as a common opening for both sets of sexual organs. Multiplication takes place by the union of two parasites, each acting as both male and female. The adult parasite usually inhabits the bile-ducts of sheep, sometimes of man, in large numbers. It may obstruct the biliary ducts, giving rise to congestion and enlargement of the liver with later on degeneration and cystic formation. A water snail may be the intermediate host.

The **Dicrocœlium (Distoma) lanceolatum** is about 8 to 10 mm. long, 2 to 2.5 mm. wide. The anterior end is the more pointed. Has two suckers, quite widely separated, and in between them is the genital pore.

The eggs are oval, about 0.04 to 0.05 mm. long.

The snout has a spread-out membrane like an umbrella.

FIG. 117.—HUMAN BLOOD FLUKE (SCHISTOMA OR DISTOMA HÆMATOBIUM). × 5 (Leuckart).
The female is partially within the canalis gynæcophorus of the male.

Is frequently found in combination with the F. hepaticum. Intermediate host unknown.

The **Schistosoma (Distoma) hæmatobium** has two distinct sexual forms, the male and the female.

The male is the larger, is from 12 to 14 mm. long and 1 mm. thick. The female is longer and thinner, 16 to 18 mm. long and 0.13 mm. thick.

The eggs are oval, 0.12 mm. long, and somewhat pointed at the ends.

In the act of fecundation the female crawls into a canal formed by the curving up of the sides of the male.

These parasites occur in the portal, abdominal, and cystic veins. The eggs are produced in great numbers and obstruct and rupture the capillaries, thus escaping into the tissues. The wall of the bladder may become inflamed, ulceration take place, and eggs and blood escape in the urine.

The embryos are supposed to live in water and gain entrance by the alimentary tract and through the skin.

The **Paragonimus westermanii (Distoma pulmonale)** is a form that has quite frequently been found in Japan and China.

Is 8 to 10 mm. long, 5 to 6 mm. wide. Resembles quite closely the liver fluke.

Is found in the lungs, usually near the periphery of a cavity. These cavities contain a muco-purulent liquid in which are found many eggs.

Nematodes, or **round worms,** are long round parasites, are not segmented, are provided with alimentary organs, and the sexes are separate.

The life-history, with the exception of the trichina, is completed within a single host.

The **Ascaris lumbricoides** is the commonest intestinal parasite in man. The female may be 40 cm. long and 5 to 6 mm. thick; the male 25 cm. long and 2 to 4 mm. thick.

The body is brownish and has four longitudinal ridges extending the entire length. The head has three rounded lips, between which is the mouth.

The alimentary canal runs through the entire worm to an opening on the hinder abdominal surface.

The sexual organs occupy the posterior half of the body, the sexual opening being at the junction of its anterior and middle thirds. The uterus is double, thread-like, and twisted; may contain millions of eggs, which are from 0.05 to 0.06 mm. long, are oval, and are covered by a layer of clear albuminous matter which preserves them for a long time after being extruded.

An intermediate host is not needed, the eggs developing in the human intestine. They may occur singly or in numbers. Are found in the small intestine, but may migrate, entering the gall-ducts, the stomach, the esophagus, and even the larynx or nasal cavities.

May obstruct the intestine, or set up inflammation with perforation and abscess formation. Also cause obscure nervous symptoms.

The **Oxyuris vermicularis**, *Thread* or *Seat worm*, is commonly found in children.

Is white in color; the female is from 10 to 12 mm., the male 2.5 to 5 mm. long. The tail of the female is long and tapering, that of the male blunt and curved upon itself. The mouth lies between three lips. The genital pore is anterior in the female, posterior in the male. The eggs are oval, about 0.005 mm. long, and contain embryos with sharp posterior ends.

FIG. 118.—ASCARIS LUMBRICOIDES (FEMALE) (Mosler and Peiper).

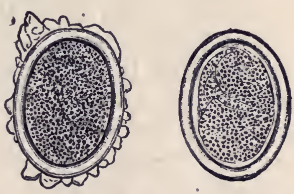

FIG. 119.—EGGS OF ASCARIS LUMBRICOIDES (Mosler and Peiper).

The parasites live in the large intestine, usually in great numbers. May leave the rectum and enter the vagina and urethra in girls, causing much irritation and itching. The eggs are swallowed, hatch in the upper intestine, and the female worms becoming fecundated form more eggs.

The **Eustrongylus gigas** is a large round worm found in the

pelvis of the kidney or ureter, usually in horses or cattle, but sometimes in man. The female is about one meter long and 8 to 12 mm. thick, the male about one-third as long. Is reddish in color, the anterior end is retracted, and around the mouth are six papillæ. In the male the posterior end is expanded, and a spicule projects from the cloaca.

The **Filaria medinensis,** or "Guinea-worm," is a very slender round worm about one meter long. The female only is certainly known. It has a circular oral opening with four hooklets. The tail is sharply pointed.

The greater part of the worm consists of a uterus which contains enormous numbers of embryos. These escape, especially when water is brought in contact with the ulcer from which the worm extrudes. The embryos live in the water, and one view is that a minute crustacean is the intermediate host.

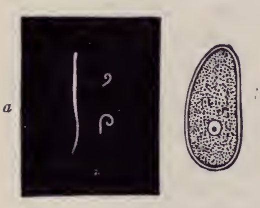

FIG. 120.—OXYURIS VERMICULARIS AND EGG (after Heller).

a, Natural size; *b*, egg.

This worm is found in the tropics and occurs in the subcutaneous tissues, particularly of the feet and hands.

The **Filaria sanguinis hominis (Filaria bancrofti),** as commonly found, is the embryo of a worm that is rarely seen in the adult form. The usual form is the *Filaria nocturna*. The adult is from 8 to 10 cm. long and lives in the larger lymphatic vessels. No eggs are laid, but great numbers of living embryos are set free in the lymphatics and thence into the blood. The embryos are about 0.25 mm. in length, and the diameter a little greater than that of an erythrocyte. The head is broad and blunt, the tail tapering. They appear in the blood only during the period of rest. If the person works at night and sleeps during the day, they will be found during the latter period.

They escape through the kidneys into the urine in attacks of hematuria.

The mature worm, from obstruction to the lymphatics, may

give rise to marked enlargements, such as lymph-scrotum and elephantiasis.

The *Filaria perstans* is a form that is found in the blood at all times, day or night. The embryo alone is known. The *Filaria diurna* occurs in the daytime only.

Filariasis is common in Egypt, India and Africa, and the intermediate host is a mosquito, one of many species belonging to several genera.

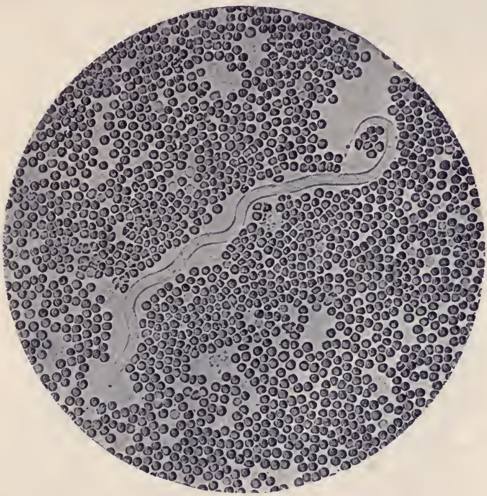

FIG. 121.—EMBRYO OF FILARIA BANCROFTI. MICROFILARIA BANCROFTI. Living specimen (Bulletin No. 1, Medical Department, U. S. Army).

The **Uncinaria (Anchylostoma) duodenalis** is a small round worm found in the upper intestine of man. The male is from 7 to 11 mm. long and 0.46 mm. wide, the female from 7 to 16 mm. long and 0.63 mm. broad. The head of the worm is cylindric and bends backward. The mouth has three pairs of sharp incurved hooklets and opens directly into an esophagus that occupies the anterior third of the worm.

The posterior end of the female is pointed and has two openings, the excretory and the genital pore. The tail of the male is expanded and is arranged like a three-leaved cup.

The eggs appear in the feces as oval, thin-shelled, and doubly contoured bodies about 0.36 to 0.63 mm. long. The number of eggs is enormous. Has been estimated that more than four millions may occur in a single stool. After exposure to the air the embryos escape from the eggs in about six days and continue their existence in the water. They may gain entrance by means of drinking-water or, as has been shown, the embryos may penetrate the skin of the feet.

The adult worm may occur in small or large numbers. It attaches itself to the wall of the intestine and sucks the blood

Fig. 122.—Uncinaria Duodenalis (von Jaksch).
a, Male, natural size; *b*, female, natural size; *c*, male, magnified; *d*, female, magnified; *e*, head, greatly magnified; *f*, *f*, *f*, eggs.

for its nourishment. If the worm lets go, there remains an area of ecchymosis with a small point of hemorrhage in the center. It is thought that the parasite may inject into the wound some substance that interferes with the coagulation of the blood.

If the organisms occur in great numbers, the loss of blood may be so severe as to cause a very marked anemia.

This condition exists in Egypt, southern Europe, and Brazil.

The **Necator (Uncinaria) americana** is a closely related worm that is widely distributed in America, particularly in the sandy soil of the southern States. It has a much smaller head, smal-

ler and blunter teeth, and is less dangerous than the European variety.

The **Strongyloides stercoralis (Anguillula intestinalis)** is a very motile worm, about 2 mm. long, and very thin. Is found in the intestine. The embryos were thought to be a different form of parasite and were formerly called *A. stercoralis*. Occurs in China and is found in some cases of diarrhea. The **Trichuris trichiura (Trichocephalus dispar)**, or "whip worm," is found in the large intestine of man, but is of little pathologic importance.

Fig. 123.—Trichocephalus Dispar (Heller).

a, Female; *b*, male (natural size).

Is from 4 to 5 cm. long and is peculiar in that the anterior two-thirds are very slender, while the posterior third is thicker.

Fig. 124.—Eggs of Various Worms Found in the Alimentary Canal of Man. × 400 (Mitchell).

A, Ascaris lumbricoides; B, C, Oxyuris vermicularis; D, Trichocephalus dispar; E, Uncinaria duodenale; F, Fasciola hepatica; G, Dicrocœlium lanceolatum; H, Tænia solium; I, Tænia saginata; K, Dibothriocephalus latus.

In the male the posterior portion is spirally coiled, in the female is slightly curved.

The eggs are about 0.55 mm. long and at each end have a button-like excrescence.

The **Trichinella (Trichina) spiralis** is a very important parasite that undergoes development in two hosts.

It occurs in two forms in man and the lower animals, as an intestinal fully developed worm and as an encapsulated embryo in the muscular tissue. Is most common in hogs. The adult female is from 2 to 4 mm., the male 1.5 mm. in length. The eggs develop into embryos while within the mother. When an encysted embryo is taken into the stomach the gastric juices dissolve the shell, and the parasite is set free. It very rapidly matures, and in the course of from five to seven days eggs are discharged. Within a few days a couple of thousand embryos will have been liberated. These young parasites penetrate the walls of the intestine, gain entrance either into the blood or the lymphatics, most probably the blood, and in the course of about ten days become lodged in the voluntary muscles.

FIG. 125.—FRESH MUSCLE TRICHINÆ (Mosler and Peiper).

In the muscle fibers the embryos become encysted in two to three weeks. There is a deposit of lime salts around the curled-up embryos which may either die and become calcified or remain alive for years. The encysted form appears as a small white point.

Infection in man takes place by the eating of meat (measly pork) that contains the trichinæ and that has not been properly cooked. A temperature of 65° C. kills the parasite, but pickling and smoking destroy those only which are in the superficial parts, those deep within being unaffected.

When the embryos escape from the cysts into the intestine severe vomiting and diarrhea may occur. During the emigration to the muscles the symptoms are those of muscular rheumatism. In this disease there has frequently been noticed a very great increase of the eosinophile cells in the blood.

ARACHNOIDEA

The insects are external parasites which may prove dangerous by means of their own metabolic products, by acting the part of intermediate host for some parasite, or by mechanically carrying the source of infection.

The first class is not very important. In the second is the mosquito, which may in some of its varieties transmit malaria, yellow fever, or filaria sanguinis hominis.

Flies may mechanically convey typhoid bacilli from feces to articles of food.

CHAPTER XV

POST-MORTEM EXAMINATION

The purpose primarily of post-mortems is to determine the cause of death. Frequently there are found several diseased organs. The question then arises as to the order in which they were involved and from what their condition resulted.

The examination may be divided into the inspection of the external appearances and into the examination, both macroscopic and microscopic, of the internal organs.

During the post-mortem there should be some one to take notes on the various findings. If possible, the clinical history of the case should be learned before the autopsy is begun.

EXTERNAL INSPECTION

The appearances should be carefully noticed, as they are of great importance, particularly in medico-legal cases, such as approximate age; sex; height, measured as the body lies on its back between two uprights; bodily development; condition of nutrition; general condition of the skin; amount of fat present.

Distinguishing marks; irregularities of the teeth, deformities of any kind; fractures; wounds, whether ante-mortem or post-mortem. If the former, there may be indications of bleeding, edges will gape, and there will be some signs of inflammation or beginning repair. If post-mortem injury, there will be no escape of blood into the tissues, no bleeding on incision, no inflammation or repair.

Presence of edema, most common in the lower extremities at the ankles, the scrotum, and labia.

Signs of decomposition, first appearing as a greenish discoloration of the abdomen and prominence of the superficial veins due to the staining of the tissues by blood-pigment from degenerated erythrocytes.

Rigor mortis, its degree and extent; post-mortem lividity, or hypostases, is present in dependent parts and disappears on pressure; diffuse pigmentation, the result of decomposition, does not disappear on pressure.

The condition of the pupils, whether dilated, contracted or unequal; the sclera; size and shape of thorax; distention or retraction of abdomen.

INTERNAL INSPECTION

The generally accepted order of examination is brain, spinal cord, thorax, and abdomen. The brain should be examined first, so that the amount of blood in the cerebral vessels can be determined. As in this country autopsies are usually limited to the thorax and abdomen, they will be first described.

The autopsy should not be done by artificial light, as the color values are distorted.

The operator should stand on the right side of the body and should grasp the handle of the knife as he would in cutting bread. The knife should be drawn and not pressed or shoved into the tissues. The main movement should come from the shoulder, the secondary from the elbow-joint.

Incisions into organs should be deep and single rather than shallow and numerous, as a broad surface gives much more information than a narrow one.

The primary incision is a long single one extending from the larynx along the median line to the pubes, passing to the left of the umbilicus so as to avoid the round ligament of the liver. The knife should be held almost horizontal so that the belly and not the point is used.

Over the sternum the incision extends to the bone; over the abdomen it should go only as deep as the subcutaneous tissue or the muscle. The abdominal cavity is opened by making a small incision through the peritoneum a little below the xiphoid cartilage. Two fingers of the left hand are inserted, the flaps drawn upward, and the incision continued between them down to the pubes. The recti muscles may be divided just above the pubes, care being taken not to cut the skin.

The abdominal flaps in turn are seized with the left hand and strongly drawn outward. This renders the tissues tense and they are dissected away from the ribs by long sweeping cuts. The operation begins over the lower border of the ribs and is carried up a little above the articulation of the clavicle and outward as far as the anterior axillary line.

The abdomen should then be inspected, first without touching anything. The organs and their relations should be noted; the character and the amount of any fluid present and any that runs off should be caught and measured. The omentum should be removed and the intestines examined, also the appendix and the mesenteric lymph-nodes. The peritoneum normally is smooth, glistening, and transparent, the same as any serous membrane.

The height of the diaphragm is determined by introducing the hand under the costal margin and finding at what rib or interspace the muscle reaches in the mid-clavicular line. On the right side it is usually about the level of the fourth rib or interspace, on the left is about the third rib or interspace. If the diagram is lower than normal it generally indicates fluid in the pleural cavity, enlargement of the thoracic organs or new growths.

Before opening the thoracic cavity, if pneumothorax be suspected raise the skin flap and fill the pocket thus formed with water. Puncture below the level of the water and watch for bubbles to come through.

The thorax is opened by cutting through the costal cartilages, from the second down, by holding the knife almost horizontal and resting it on the rib in advance before the previous one is completely severed. The division should take place at the junction of the rib and cartilage. Instead of using a knife the intercostal spaces may be first opened and the ribs then divided by means of the costotome. By this method there is less danger of cutting into the lungs.

The sternum is elevated by grasping the xiphoid cartilage; the attachment of the diaphragm is divided on either side. It is freed from the underlying tissues by long cuts of the knife, which should be made close to the bone so as to avoid the

pericardium. When the first rib is reached its cartilage is divided about 2 cm. further out than that of the second. The edge of the knife should be directed upward and outward, the handle being beneath the elevated sternum.

The clavicle may be disarticulated by cutting from below along the irregular line of the sterno-clavicular articulation. By this method there is less danger of wounding the large vessels at the base of the neck, a very important point in medico-legal cases. The articulation may be divided from above by entering a narrow knife along the line of the joint, which curves down and out. The handle of the knife should incline so that it is nearer the cadaver's chin than is the blade. If held perpendicular both the clavicle and sternum interfere, as the joint slants. If properly carried out, it can be done without any great force being exerted, short up and down strokes being used. The sternum should then be twisted out rather than cut, otherwise the large vessels of the neck may be divided.

If the cartilages have become calcified, care should be taken not to cut one's hands on the exposed ends. Protection can be had by drawing the dissected flap of skin over the edges.

If removal of the sternum is not allowed, the thoracic organs may be removed from below by separating the diaphragm from the ribs.

On removal of the sternum, the lungs and the pericardial sac are exposed. One should notice how near the lungs come to meeting in the median line. Ordinarily they will touch at the level of the second rib.

The pleural cavities should be examined. One should determine the presence or absence of fluid, its character and amount. Adhesions should be looked for, and the amount of force required to break through them is a guide as to their duration. If the adhesions are very dense, the best way when one comes to remove the lungs is to strip off the costal layer of the pleura with the viscera.

In opening the pericardium the sac is picked up by the fingers and an incision made upward to where the large vessels enter at the base of the heart. This cut is continued

downward to the lower right border. From the middle of this incision one is made down to the apex. The cut should be made from within out, so as to avoid wounding the heart.

By lifting up the apex of the heart the amount and character of the contained fluid can be determined. Is usually only 5 to 10 c.c.

The presence or absence of adhesions between the heart and pericardium should be noted. Sometimes the entire cavity may be obliterated.

Before making any incisions into the heart, its size, shape, and position should be noted. The distention or contraction of the various cavities should be determined.

Opening of the Heart.—Weight 304 gm. This may be done either *in situ* or after removal from the body. As a general thing, it is best to remove the heart before making any incisions. It is then easier to make the openings, but there is more danger of bacterial contamination occurring.

To remove the heart one grasps the apex with the left hand and lifts up the entire organ. By three or four long cuts made from below upward, first severing the inferior vena cava, then the left pulmonary vein, and finally the remaining vessels, the heart is removed. Care should be taken to wound neither the auricles nor the underlying esophagus.

In opening the heart the primary incisions are made with a knife and then united by using long straight scissors with blunt points or else a cardiotome.

The heart is then placed in a position corresponding to its normal one within the body; the apex directed toward the operator, the anterior surface being upward. The cavities are then opened in the order in which they receive the blood.

The *right auricle* is opened by making an incision from the inferior to the superior vena cava and then continued into the auricular appendage.

In opening the *right ventricle* the first cut extends through the tricuspid valve down to the end of the cavity. The second incision is made about the middle of the primary one and at almost right angles to it. This cut should be high enough up to avoid cutting through the insertion of the anterior pap-

illary muscle. It is continued through the pulmonary valve, following along a slightly marked ridge of fat; by so doing the orifice is opened between the left anterior and the posterior leaflets.

The *left auricle* is opened by uniting the four pulmonary veins and continuing into the auricular appendage.

The *left ventricle* has the first incision made through the mitral valve between the two papillary muscles along the left border of the heart to the apex. The second incision is made by beginning at the apex at the end of the first and continuing upward close by the interventricular septum and parallel to the anterior coronary artery. The upper end of the cut should pass about midway between the pulmonary orifice and the left auricular appendage. An aortic leaflet is generally divided in so doing.

As the auricles are opened the clots should be removed and the valves carefully examined. The size of the opening should be noted, so as to determine whether or not stenosis or dilatation exists. The test of valvular competency by filling the cavity with water is unreliable.

The ventricles are freed from blood and their valves examined.

The anterior coronary artery is examined by opening with a pair of probe-pointed scissors. The posterior coronary is best seen by placing the tip of the left forefinger over the orifice of the vessel in the aorta, then cutting from without toward the finger-tip until the artery is reached. By so doing the aorta is not injured.

The heart should be weighed, its walls measured, the condition of the valves and muscle noted, and the aorta above the valves examined for atheroma.

Lungs.—Weight 1172 gm. In removing the lung all adhesions should be broken up or cut through. It is then drawn forward and downward, the root being grasped from above between the fingers of the left hand. The primary bronchus is divided behind the left hand and the lung is lifted upward, the remaining attachments being divided.

If there are dense adhesions between the lung and the dia-

phragm, it is best to remove the latter with the lung by cutting through the attachments to the ribs. Be careful to avoid wounding either esophagus or aorta.

The two organs can be distinguished from each other by remembering that the anterior edge is thin while the posterior is rounded and the bronchi are on the inner surface. Also that the right lung has usually three lobes, the left two only, although variations occur.

The lungs may be opened by either a long incision extending from apex to base or by a horizontal incision taking in the entire width of the organ. The bronchi and blood-vessels should be opened with small scissors.

The cut surfaces should be carefully examined, the color, amount of blood, presence of fluid, solidity, degree of crepitation, smoothness, and friability noted. Portions of the more solid areas should be placed in water to see if they will float.

More room for the examination of the abdominal organs can be gained by cutting through the diaphragm on either side of the liver and turning that viscus upward.

The **spleen** is removed by drawing it gently toward the mid-line and the vessels cut close to the hilum. If adherent to the diaphragm, care should be taken that its capsule is not torn.

Its size, shape, and density should be noted, as well as the appearance of the capsule, trabeculæ, blood-vessels, lymph-follicles and pulp. Weight, 200 gm.

Intestines.—The intestines are removed next. The omentum may either be removed when the abdominal cavity is inspected or left till later. It is freed from the transverse colon by dividing it close to the gut with a knife.

The most convenient way to dispose of the intestines is by freeing the sigmoid flexure from the mesocolon and dividing just above the rectum. The transverse colon is freed by dividing the two folds of the lesser omentum, the ascending by dividing the mesocolon.

To remove the small intestine it should be grasped with the left hand and sufficient force exerted to keep the mesentery in a state of tension. The blade of the knife is held parallel to the

intestine and the mesentery is cut at its attachment by means of to-and-fro motions. As the intestines are set free they should be received into a pan. When the duodenum is reached it is ligated and cut on the distal side. The mesentery is then removed. The gut is then opened, the large intestine along one of its longitudinal muscular bands, the small along its mesenteric attachment, as opposite to that side the most important lesions involving the lymph-nodes and Peyer's patches are found.

In order to determine whether or not there is any obstruction of the hepatic or common bile-ducts the duodenum should be opened *in situ.* The incision should be along the anterior wall and extend from the pylorus to where the duodenum passes beneath the mesentery. The opening of the bile-duct is usually marked by a small papilla. Pressure is first made on the common duct, and the opening watched to see if any obstruction prevents the escape of bile. Pressure should then be made upon the gall-bladder to see if its contents can escape.

The **kidneys** may be removed along with the adrenals by making an incision to the inner side and then above the adrenal, then cutting along the outer convex border of the kidney through the peritoneum and the perirenal fat. The kidney is shelled out by using the left hand and the vessels are cut from above downward and as near to the aorta as possible. When they are divided the organ is raised and the tissues loosened with the fingers until the ureter is disclosed, when it is severed.

When the entire urinary apparatus is diseased all the organs may be removed together by first dissecting the ureters till the bladder is reached, then turning the kidneys downward, after which the pelvic organs can be taken out.

Sometimes the kidneys may be removed without the adrenals, in which case the latter are either opened *in situ* or removed separately. The right adrenal is attached to the under surface of the liver and must be dissected free.

The left kidney is generally removed first.

In examining the kidney it is held between the thumb and

fingers with the convex surface upward. A deep longitudinal incision is then made down to the hilum. The capsule can then be stripped by getting hold of it with the thumb-nail.

The size, color, condition of the surface, and density should be noted. Portions of the kidney substance may be removed with the capsule. The presence of cysts or of infarcts should be determined. On section the relative proportion between cortex and medulla, the color of the cut surface, the presence of abnormal substances, amount of connective tissue, the normal markings of the kidneys, the blood-vessels, glomeruli, the tubules of the cortex and of the medulla should be carefully noted. The pelvic mucous membrane should also be examined. Weight, right kidney 131, left 150 gm.

The **liver** is removed by raising up the right lobe and freeing it from all attachments, then the left lobe. If adherent to the diaphragm, remove it with the liver. The portal vein and the common bile-duct should be examined.

The tissue is exposed by one or more long cuts on the anterior surface across both lobes. Should note the amount of congestion, the degree of fatty changes, the amount of connective tissue present, and the degree of bile staining. Weight 1612 gm.

In removing the **stomach** a portion of the duodenum is cut through and lifted up and the stomach, together with the pancreas, freed by incisions from below upward. The stomach is dissected free from the pancreas and opened along its greater curvature. If any marked lesions are noticed from the outside, the incision should be so made as not to damage them.

The **pancreas** is examined by making numerous transverse incisions. Should be on the lookout for fat necrosis. The duct may be slit open along its course.

In removing the **organs of the neck** it is best, if allowed, to continue the skin incision up to the symphysis of the jaw. The skin is dissected free as far as the hyoid bone and upward to the chin. The tissues are loosened by passing the knife around inside the clavicles. The head should be allowed to drop back and a long thin knife is inserted at the symphysis beneath the tip of the tongue. By means of a sawing motion

the muscles are divided first on one side and then on the other as far as the vertebral column. The esophagus and the trachea are lifted up and the dissection continued till the posterior wall of the pharynx is divided. The tongue is drawn downward and an incision made on either side, well out, so as to divide the lateral pillars of the fauces without wounding the tonsils. The soft palate is separated and the structures removed.

The esophagus is opened by being cut along its median line posteriorly from the pharynx down. It is then pulled to one side, when the larynx and trachea are divided along the posterior wall.

The lobes of the thyroid gland should be cut in their long diameters.

The **pelvic organs** are removed by dividing the peritoneum along the brim of the pelvis and dissecting it with the fingers till the posterior surface of the rectum is freed. The cut end of the rectum is drawn upward and toward the pubes while the attachments posteriorly are dissected away. The pelvic organs are now attached only at the external openings. These are divided anteriorly close to the pubes and posteriorly along the outlet of the pelvis.

The **rectum** is opened along its posterior wall and cleaned.

In opening the **bladder** a slight incision is made in the anterior wall of the fundus and with a pair of scissors the cut is continued along the anterior wall through the urethra.

The **uterus** is opened by making an incision along the anterior wall from the fundus to the cervix. Two secondary incisions extend from the upper end of the first cut to the openings of the Fallopian tubes. The *vagina* is opened by carrying the incision downward. It should be done from this direction so that the operator may be sure that any foreign substance found in the uterus was not conveyed there on the point of his scissors, an important consideration in medico-legal cases. The ovaries are opened along their greatest diameter.

The **testicles** can be drawn up through the internal ring and examined without any injury to the scrotum. The greater portion of the penis can be removed by incising the skin as far

as the middle of the dorsum and dividing just behind the corona. Is then dissected free and withdrawn underneath the arch of the pubes.

The structures now left for examination are the inferior vena cava, the thoracic and abdominal aorta, the iliacs and the thoracic duct. They should be slit open.

Removal of the Brain.—Weight, men 1360 gm.; women 1220 gm. To displace the scalp an incision is carried over the vertex from the tip of one mastoid process to the tip of the other. This should be made from within outward, as by so doing the hair will be divided but not cut. The periosteum should be cut through and the two flaps dissected free. The anterior one extending nearly to the orbits, the posterior is carried backward to the occipital protuberance.

The temporal muscle should be left, but is divided at the point where the cut of the saw is to be made.

The line of opening the skull extends from a point just behind and above the ear, forward over the frontal eminences to a corresponding point on the opposite side. By carrying this line posteriorly over the occipital protuberance the path of the incision is marked out. The incision is started over the forehead and carried backward over the line mapped out. By bracing the saw with the thumb of the left hand and drawing backward a correct start can be made. Continue the incision, first on one side and then on the other, till the mastoid processes have been reached. Care should be taken not to injure the dura. Is often best not to cut through the inner plate of the skull but to break it with a chisel. A posterior incision is continued backward a little above the occipital protuberance.

It should be noted that there are four points where the skull is particularly thick and two where it is very thin. The thick points are over the mastoid processes and in the median line anteriorly and posteriorly. The thin points are over the temporal fossæ, where the skull is so thin that a few blows with a chisel will complete the separation.

By inserting the end of a chisel in the mid-line anteriorly and then twisting it the calvarium will be loosened sufficiently

to allow the inserting of a hook. By pulling, the skull-cap will be freed unless there are dense adhesions between it and the dura. It is sometimes necessary to remove the calvarium together with the dura.

To remove the dura insert a small knife and cut from within outward along the line of the saw incision. Reflect the two flaps along the mid-line and examine the surface of the brain. The convolutions should be round and not flat. The dura is freed from its attachment to the crista galli and dissected backward. It is separated from the pacchionian bodies, to which it is adherent, by means of slight cuts. The membrane should be examined carefully and the longitudinal sinus opened. The dura should not be cut through posteriorly but should hang down.

The pia is now exposed and the external appearances of the brain should be noted; the degree of congestion, the presence of edema, of tubercles, purulent collections and local or general thickening.

The brain is removed by gently elevating the frontal lobes until the optic nerves are seen. Care should be taken not to cut the olfactory nerves. The optic nerves are cut as far forward as possible, then the carotids are severed.

The tentorium is cut by a sawing motion close to its attachment to the petrous portion of the temporal bone. The various cranial nerves are then divided.

The spinal cord is severed by inserting the scalpel as far as possible into the spinal canal and cutting through with an oblique incision from one side to the other. At the same time the vertebral arteries are cut.

The brain during this should be supported by the left hand.

The base of the skull should be examined, and if a fracture is suspected the dura is stripped off.

To examine the brain place it on its vertex with cerebellum toward one. The pia and the cranial nerves should be examined. Then carefully note the arteries for changes in size, malformations, presence of atheroma, aneurysms, or of tubercles. Separate the Sylvian fissure and examine the vessels

there as tubercles, emboli, aneurysms, and hemorrhage may be discovered although absent elsewhere.

To section the brain the following method is generally employed: The brain is placed on its base and the hemispheres separated till the corpus callosum is exposed. The first incision is made into the lateral ventricle about 3 mm. from the median line of the corpus callosum and extending into the anterior and posterior cornua. Posteriorly the convolutions over the cornua are cut through. A series of incisions are made through the hemisphere just external to the basal ganglia with their edges coinciding but going at an angle of about 45 degrees. This gives a number of wedge-shaped portions, held together by the pia, which should not have been removed.

The brain is turned half around and the process repeated on the other side. Care must be taken not to injure the ganglia when opening the ventricle.

The corpus callosum is gently lifted and divided by passing a knife through the foramen of Monro and cutting from below upward. The cut portions are reflected, exposing the velum interpositum and the choroid plexus. The third ventricle is disclosed by drawing back the velum interpositum.

The vermiform process is cut through, opening the fourth ventricle; the aqueduct is cut and all the ventricles are exposed.

The corpora quadrigemina are found by dividing the right posterior pillar of the fornix and reflecting it to the left.

The basal ganglia are exposed by making a series of transverse cuts, the brain being supported from below by the left hand.

The pons and medulla are cut transversely into thin sections.

The cerebellum is divided along the median line into two halves, each of which is subdivided by a series of incisions at right angles to the primary cut.

This method is the one that is employed when the organ has to be examined when fresh. In this way, however, the relations of the different parts may be much disturbed. The best way is to harden the entire brain, either in Müller's fluid or in formaldehyde. When hardened a series of incisions is

made transversely through the entire thickness of the organ and extending from one end to the other.

In cutting into the fresh brain the blade of the knife should always be wet so as to prevent its adhering. As long as the pia has not been divided the brain can be restored to its normal form by replacing the wedge-shaped pieces.

The middle ear and the orbits are exposed by breaking through the roof. In removing the eye the anterior half should be left and the space filled with cotton. The incision is made just posterior to the conjunctival margin and the optic nerve should be removed with it.

Removal of the Spinal Cord.—This may be done either before or after the abdominal and thoracic cavities have been examined.

The body is placed prone with the head over the edge of the table and a block under the abdomen so as to lessen the lumbar curve. An incision is made from the occiput to the sacrum along the spinous processes. The skin and muscles are dissected away on either side, exposing the laminæ at the bottom of the groove, which should be thoroughly clean. By means of a double- or single-bladed saw the laminæ should be divided so as to enter the spinal canal at its outside limits. The laminæ of the cervical vertebræ are more easily bitten through with strong bone forceps.

Divide the spinous processes on either side, cut the ligaments in the lower lumbar region, and lift them up to the neck.

The dura over the cauda equina is picked up with forceps and the nerves are cut from below upward; if done carefully, the posterior root ganglia can be removed with the cord. At no time should the cord be pulled or bent.

The dura should be opened by a longitudinal incision, made with probe-pointed scissors, either along its anterior or posterior surface. Transverse sections of the cord, about 2 cm. in thickness, should be made; the incisions coming in between each two pair of nerves and leaving the segments attached to the pia.

A diagnosis is frequently made with difficulty from the fresh macroscopic appearance of the cord.

CHAPTER XVI

LABORATORY TECHNIC

EXAMINATION OF FRESH MATERIAL

THE examination of fresh material may be made by teasing the tissue in water or, preferably, 0.6 per cent. saline solution. This, however, may not be satisfactory unless the tissue has been allowed to remain in some fluid long enough for the cells to become separated from the basement membrane. This is known as *maceration;* the following fluids are used for this purpose:

1. Alcohol, 33 per cent. (Ranvier), in which soak the specimen twenty-four hours.

2. Very weak chromic acid solutions, 1 : 10,000, or its salts. Müller's fluid is especially useful for nervous tissue. Leave in the acid twenty-four hours; in the latter, three to five days.

3. Osmic acid, 1 per cent., for twelve to twenty-four hours. Is useful if there is any fat present.

4. Potassium hydrate, 33 per cent., for from fifteen to twenty minutes. The specimen should be examined in the same fluid, as water distorts the cells. To preserve the tissue, wash in 50 per cent. acetic acid, then in water, and after staining in alum carmin can be mounted in glycerin. Is good for the examination of tissues or tumors that contain smooth, involuntary muscle-fibers.

5. Arnold's method: The small pieces of tissues are placed for five to ten minutes in 1 per cent. acetic acid, then for twenty-four to forty-eight hours in the weak chromic acid solution. They may finally be stained with picrocarmin.

Various reagents may be used in the examination of fresh specimens to render them transparent, to bring out certain details, or to cause various substances to disappear:

1. Glycerin clears the tissues and has the advantage of not

changing chemically nor getting thin. Permanent mounts may be made by sealing the edges of the cover-glass with paraffin.

2. Potassium acetate in a saturated watery (50 per cent.) solution has a clearing action similar to, but less marked than, glycerin.

3. Acetic acid: Has the advantage that it causes the nucleus to shrink and the connective tissue to swell and become transparent. It does not affect fat, but dissolves the protein granules, so differentiates the two processes. Elastic fibers and micro-organisms are unaffected, so stand out prominently against the changed connective tissue. The acid may also be used to dissolve calcium salts. Solutions of 1 to 2 per cent. are generally employed, but the pure glacial acetic acid may be used.

A solution of acetic acid with fuchsin may be employed and in that way stain the nuclei.

4. Weak watery solutions of iodin. The following solution (Lugol's) is mixed with 3 to 5 parts of water:

Iodin	1
Potassium iodid	1
Distilled water	100

This brings the nucleus and the cell contour more plainly to view and also stains glycogen and amyloid particles brown.

5. Potassium and sodium hydrate solutions of from 1 to 3 per cent. have the power to dissolve most tissues, but do not affect elastic tissue, fat, bone, pigment, bacteria, or amyloid. Thirty-three per cent. solutions dissolve the cement substance and isolate the cells. This reaction takes place in a few minutes.

6. Osmic acid in 1 per cent. watery solution will stain fat black or brown.

7. Hydrochloric acid in from 3 to 5 per cent. is used for the recognition of lime salts, either in bone or in the tissues which it dissolves, with the production of bubbles of CO_2.

8. Fresh preparations may be stained by allowing a few drops of watery stains to pass under the cover-glass and then washing out the excess. Methyl-green, Löffler's methylene-

blue, or acetic acid fuchsin may be used. Hematoxylin is unsuitable.

FIXATION AND HARDENING

If a more exact examination is desired, the tissues must be hardened and fixed. The material should be placed in the fluid used as soon as possible after it has been obtained. The point desired is that the conditions as they exist in the tissues during life shall be retained.

The different solutions vary greatly in their power of penetration and also in their effects upon different tissues. The action is facilitated by cutting the specimen in small pieces. After fixing and hardening it is generally necessary to thoroughly wash, so as to remove all traces of the agent employed.

The points to be observed are:

The specimens should not be more than 2 mm. in thickness.

The volume of reagent used should be from ten to fifteen times larger than the bulk of the specimen.

Place a layer of absorbent cotton or filter-paper in the bottom of the jar, so that the tissue may be acted upon by the fluid from all sides.

After sufficient hardening, remove the specimen and wash it in running water for twelve to twenty-four hours. It is then passed through alcohols of various strengths—70, 80, and 90 per cent., about twenty-four hours in each.

1. **Alcohol.**—It is used for rapid work and particularly if bacteria are suspected. It is not good for nervous tissue. Specimens should, as a rule, be put in weaker alcohol before being placed in absolute. This method is not used as much as formerly, on account of the shrinking and distortion of the tissues and the destruction of the red blood-corpuscles.

The so-called absolute alcohol is usually little more than 95 per cent. To extract the water, copper sulphate should be heated until the blue color disappears and then added to the alcohol. The alcohol should be filtered before using and the copper sulphate reheated when it begins to turn blue.

2. **Formalin.**—This reagent is being used very greatly in place of alcohol. It has numerous advantages. The harden-

ing takes place rapidly, the erythrocytes and other pigments retain their natural colors.

As formalin is bought it consists of a 40 per cent. solution of formaldehyd in water. The strength commonly used is a 1:10 or a 4 per cent. solution.

The tissues are left from four to six hours in the 4 per cent. solution, then thoroughly washed in water, and finally passed through alcoholic solutions of varying strengths.

Formalin is also used in combination with other mixtures, particularly as Orth's solution. This is made by adding 10 parts of formalin to 100 parts of Müller's fluid. This should be made fresh, as in the course of five or six days there is a crystalline precipitate formed. This fixes nuclear figures very well and hardens small pieces of tissue in from three to six hours. It is particularly important that they should be very carefully washed in running water. Is good for nervous tissues.

3. **Müller's fluid** is made up of:

Potassium bichromate	2.5
Sodium sulphate	1.0
Distilled water	100.0

This should be used in large quantities and should be changed every second day for about five times, and then be replaced whenever the solution becomes cloudy. To prevent the growth of mold 1 gm. of bichlorid of mercury should be added to 2 liters of the fluid.

For thorough hardening of small objects from ten to twelve weeks is required; for a large object, like the brain, a year. The process can be hastened by placing the preparation in an incubator and frequently changing the fluid.

After complete hardening the preparation is carefully washed in water, and then run through increasing strengths of alcohol. The sections stain well with hematoxylin and eosin. The red corpuscles are well preserved.

4. **Erlicki's fluid** consists of:

Potassium bichromate	2.5
Sulphate of copper	0.5
Distilled water	100.0

This fluid has the advantage that preparations will harden

in from eight to ten days; and if in the incubator, in from four to five days. Its disadvantages over Müller's fluid are that it does not prevent shrinking as well and that there is frequently a precipitate in the tissues.

5. **Bichlorid of mercury** is of particular value in the fixation of cells and mitotic figures, but it has very little penetrating power. All the solutions that contain bichlorid have the drawback that there is a precipitation of mercury in the tissues that may be mistaken for pigment unless removed. These compounds may be dissolved by the addition of several drops of iodin to the 80 per cent. alcohol into which the specimens are put after having been washed. The iodin may be added to the alcohol in which the cut specimens are placed before being stained.

6. **Zenker's Fluid.**—

Bichlorid of mercury	5.0
Potassium bichromate	2.5
Sodium sulphate	1.0
Distilled water	100.0
Glacial acetic acid	5.0

The mercury and bichromate are dissolved in warm water and the sodium then added. It is best not to add the glacial acetic acid until the solution is ready to be used, as the acid rapidly evaporates.

After being in the fluid for twenty-four hours or less, according to the size of the specimen, it is thoroughly washed in running water twelve to twenty-four hours and then hardened in alcohol. The tissue should be passed through 80 per cent. alcohol containing iodin so as to remove the precipitate of mercury that forms.

Tissues prepared in this way stain according to all methods. The chromatin figures are well preserved as well as the erythrocytes.

7. **Osmic Acid.**—Its penetrating power is very slight, so very thin pieces of tissue, not more than 5 mm. in thickness, can be used.

A 1 per cent. watery solution is usually employed. It should be kept in the dark, and when the specimen is fixed,

well washed. The paraffin method of embedding should be employed, using chloroform or clove oil, as the celloidin will dissolve out the fat. In clearing, do not use xylol, as it also dissolves fat.

8. **Flemming's Solution.**—

Aqueous chromic acid solution (1 per cent.)........	15
Aqueous osmic acid solution (2 per cent.)..........	4
Glacial acetic acid..............................	1

The small bits of tissue are left in the fluid one to three days, well washed for several hours, then hardened in increasing strengths of alcohol. It is used for karyokinetic figures and for fat. Stains best with watery safranin.

9. **Hermann's fluid** is a modification of the above. A 1 per cent. platinum chlorid solution is used instead of the chromic acid. The nuclear figures are especially well preserved. The method of employment is the same as with Flemming's.

DECALCIFICATION

General Rules.—The tissue must be well hardened before being put in the decalcifying fluid, otherwise it will be much altered. The formalin method is well adapted and small pieces should be used.

An excess of fluid should be used and it should be frequently changed. After complete decalcification the tissue should be carefully washed for two or more days. It must then be rehardened before it is ready to cut. The tissue is decalcified if it allows a needle to penetrate without meeting distinct resistance.

The following are the fluids commonly used:

1. **Chromic Acid and Its Salts.**—Müller's fluid for small pieces of bones or embryonal bones. It is a very slow process. Can be hurried by placing in an incubator.

2. **Saturated Watery Solution of Picric Acid.**—Requires about three weeks for embryonal bones. Larger and older pieces take several months. Can be hastened by adding 3 to 5 per cent. of nitric acid. To remove the picric acid, wash the tissue, then place in 95 per cent. alcohol to which several

drops of a saturated watery solution lithium carbonate have been added. The fluid becomes colored and more carbonate should be added until it remains completely clear.

3. **Hydrochloric Acid.**—When used in 1 to 10 per cent. solution it works quite rapidly, but injures the tissues. Is best used as:

Ebner's fluid:

Hydrochloric acid	2.5
Alcohol	500.0
Distilled water	100.0
Sodium chlorid	2.5

This method can be hastened by increasing both the hydrochloric acid and sodium chlorid to 5 per cent.

4. **Nitric acid,** in from 3 to 10 per cent. in water or formalin, is well adapted for bone tissue from adults. The alteration to the tissue is less than when corresponding solutions of hydrochloric acid are used.

Haug recommends the following on account of its more rapid and better action:

Nitric acid, c. p.	30.0–90.0
Absolute alcohol	700.0
Distilled water	300.0
Sodium chlorid	2.5

5. **Phloroglucin.**—This protects the tissues from the action of the acid, so that very strong solutions may be used. It acts very rapidly: small pieces are decalcified in one-half hour; larger ones, in several hours.

A stock solution is made consisting of:

Nitric acid, c. p.	10 c.c.
Phloroglucin	1 gm.

This is carefully dissolved by warming; is best done under a hood. To this is added 100 c.c. of a 10 per cent. aqueous solution of nitric acid.

A more slowly working mixture is:

Phloroglucin	1
Nitric acid	5
Alcohol	70
Distilled water	30

Thoma's method is to:

1. Harden in Müller's fluid or alcohol.
2. Decalcify in:

Alcohol	5
Nitric acid	1

changing the solution very frequently.

3. Wash in alcohol.
4. Wash thoroughly in alcohol to which has been added an excess of calcium carbonate.

The decalcification requires from two to three weeks for large pieces. To remove the acid the tissue has to be in the carbonate alcohol from eight to fourteen days; should remain until there is no acid reaction with litmus-paper.

6. **Trichloracetic acid,** used in 5 per cent. aqueous solution and frequently changed, decalcifies in from five to seven days; generally with good results.

INJECTION

For the purpose of making them more easily studied the blood-vessels and other hollow structures may be filled with some injecting material that contains a stain. This procedure is not frequently used for pathologic purposes.

EMBEDDING METHODS

The purpose of embedding is to give to a tissue a sufficient firmness to permit the cutting of thin sections. Two methods are commonly employed—one with celloidin, the other with paraffin.

Celloidin has the advantage of not requiring heat, and can be used for larger pieces of tissue. On the evaporation of the alcohol and ether a comparatively solid mass remains.

Paraffin can be used for small pieces of tissue only. It also renders the specimen brittle, so that it is frequently difficult to cut good sections. Although fluid when kept at the necessary heat, the paraffin becomes hard on cooling.

Celloidin Method.—In this process two solutions of celloidin of different thicknesses are employed—one of the consistency of syrup, the other of that of molasses. These solutions are

made by adding to a mixture of equal parts of absolute alcohol and ether enough celloidin to give the desired consistency. The specimens must be thoroughly dehydrated in absolute alcohol and then placed in equal parts of absolute alcohol and ether for twenty-four to forty-eight hours. This latter step is not essential, but is advisable. From the alcohol the specimens are left in the thin celloidin at least twenty-four hours and in thick celloidin for a like period. If there is no hurry, the longer the time in each celloidin solution, the better will be the result. They are then placed on blocks, covered with thick celloidin, and allowed to harden. In the course of a few minutes, when the block can be turned upside down without the specimen sliding off, they should be placed in 80 per cent. alcohol. After remaining there for several hours they are ready to cut.

The blocks best adapted for use are those made out of vulcanite or hard paraffin. The latter are particularly convenient. A square of hard paraffin is cut up into blocks of various sizes and the tops roughened with a knife so as to give a better surface for the celloidin to adhere to. Cork and wood are not well adapted, as after being in the alcohol for any length of time the tannic acid is extracted; it penetrates the specimen and interferes with its staining properties.

In cutting celloidin sections the knife is clamped at a very marked slant, so that as much of it as is possible will be used. The blade and the specimen should be kept constantly wet with 80 per cent. alcohol. As the sections are cut they are lifted off the knife with a camel's-hair brush and placed in a dish containing water. This causes them to flatten out.

After the staining has been completed the sections are passed through graded alcohols to remove the water and are then placed in some fluid that will clear them. Clove oil should not be used, as it dissolves the celloidin. Bergamot, cedar oil, creosote, and xylol, alone or in combination with 1 part of carbolic to 3 parts of xylol, do not affect the celloidin.

Summary:

1. Dehydration in absolute alcohol.
2. Absolute alcohol and ether, equal parts, one to three days.

3. Thin celloidin, one to five days.
4. Thick celloidin, one to five days.
5. Mount on block.
6. Alcohol (80 per cent.), twelve to twenty-four hours.
7. Cut on microtome.
8. Stain, dehydrate, and clear.
9. Mount in balsam.

Paraffin Method.—The preparation must be thoroughly dehydrated in absolute alcohol or anilin oil. It is then placed in some fluid that is a solvent of paraffin—xylol or chloroform are commonly used—for four to five hours. The fluid should be changed several times. Then it is put in a mixture of chloroform or xylol and paraffin for two to three hours. The infiltration is hastened by heating the mixture at about 50° C. It is then placed in paraffin that melts at about 50° C. for three to five hours, the paraffin having been changed once or twice. The melting-point can be varied by making combinations of paraffin that melt at different degrees. The two generally used are one of 56° C. and another of 45° C. In warmer weather a paraffin with a higher melting-point is used.

The specimen is taken and placed in a little paper box in which a small amount of paraffin has been poured. When the tissue has been properly arranged, more paraffin is added. The box is then placed in a dish of cold water, so that it will be rapidly cooled. This prevents crystallization and brittleness. Instead of using the paper boxes two right angles of metal are put on a glass plate so as to form an enclosure. Paraffin is poured in to form a thin film, then the tissue, and finally more paraffin.

After cooling, the specimen is fastened on a block of vulcanite or hard paraffin by heating its surface, and is then cut on the microtome. The blade is held at a right angle if the specimen is small, on a slant if large, and the cutting is done dry, no alcohol being used.

Summary of the paraffin embedding:

1. Dehydration in absolute alcohol.
2. Xylol or chloroform four to five hours, changing the fluid a couple of times.

3. Xylol or chloroform and paraffin, two or three hours.
4. Melted paraffin in hot chamber at 50° C. for three to five hours. Change once.
5. Block and quickly cool.
6. Cut.

The paraffin sections are so brittle that they cannot be treated in the same way as the celloidin ones. The best method is to take the section and place it in a dish containing water at about 45° C. This causes the specimen to flatten. A perfectly clean slide is then smeared with a very fine film of glycerin-albumin and is slipped under the floating section. The excess of water is drained off or carefully touched with blotting-paper and the slide is then placed in the incubator at 37° C. for three to five hours.

The paraffin should be removed before staining the section. This is hastened by holding the slide over a small flame until the paraffin becomes transparent, when it is placed in xylol or turpentine for about two minutes. From there into absolute alcohol for about five minutes. It is advisable but not necessary to put the slides into weaker alcohol before beginning the stain. When the above steps have been gone through the tissues may be stained any way that is desired.

Glycerin-albumin solution for fastening paraffin sections to the slide is made as follows: The white of an egg is well beaten and to it is added an equal volume of glycerin. These are thoroughly mixed and filtered. It is used by smearing a very thin layer on the slide, the paraffin section is placed on it and then heated up to a temperature of about 60° C. until the albumin coagulates. If the sections have been taken from water it must be allowed to evaporate before the coagulating is done. The evaporation will be hastened by placing the slides in the incubator.

CUTTING SECTIONS

Freezing Microtome.—This method is valuable for rapid diagnostic work, but sections cannot often be cut sufficiently thin to allow a careful examination of the details.

The piece of tissue used should not be more than 4 mm.

high and it must be free from all traces of alcohol. The alcohol is removed by placing the specimen in a large amount of water that is of a temperature of about 30° C.

The specimen is placed on the metal stand and a spray of ether or of carbonic acid gas is directed against the under side. The tissue is held in place by lightly pressing upon it with some flat piece of wood, as the handle of a small scalpel. Care must be taken not to freeze the tissue too hard or it will be so brittle as to break or show irregular streaks. The cut sections should be placed in 80 per cent. alcohol, as they will unroll better than if put directly into water.

The freezing method is particularly well adapted for tissues that have been hardened in Müller's fluid, as there is no change in the finer characteristics. Formalin is very useful, as it permits very good sections to be made and is employed especially in the rapid diagnosis of tumors.

A rapid method is as follows:

1. Take a small portion of the tissue that has been removed at the operation and place immediately in a 10 per cent. solution of formalin for about two minutes.
2. Freeze; put the sections into water to flatten.
3. Stain in lithium carmin two to three minutes.
4. Blot stain and mount in glycerin.

Serial Sections.—*Paraffin.*—The block containing the specimen is turned until the anterior and posterior edges are parallel; as much of the paraffin being removed as is possible. The knife is placed at right angles and with rapid strokes the sections are cut. The edges of the sections cling to each other and long ribbons may be cut. These ribbons should be carefully placed on sheets of toilet paper, carefully numbered and marked, so that the beginning of each series can be determined. The ribbons are divided into lengths convenient for placing on the slide. They are then floated on water and picked up on the slide covered with the glycerin-albumin.

STAINING

The principle of staining depends upon the different affinity of certain portions of the tissue for special dyes, so that they

become more evident for purposes of study. There are certain stains which show a distinct affinity for the nuclei, while others select the cell protoplasm and the intercellular substance. By employing two stains a double coloring is obtained. In some conditions a single color may affect different portions of the tissue differently.

According to their reaction, stains are divided into the basic, which are commonly nuclear or chromatin stains, and the acid, those that affect the cell protoplasm or the intercellular tissue. Neutral stains are generally artificial combinations of some of the above two.

After being stained it is generally well to differentiate. Although a stain may be a nuclear one, yet there is usually some effect upon the other substances, the same holding true in regard to the acid stains. To remove this color, certain fluids are used, as water, weak solutions of acid in water or alcohol, alcohol, anilin oil, and tannic acid.

It is also necessary that the sections shall be rendered transparent, and this is brought about by placing them in xylol, carbol-xylol, oil of cloves, creosote, or bergamot.

Certain general rules should be observed:

1. All staining fluids should be filtered before use to avoid precipitates in the tissue. Good stains should be used; the best being those of Dr. Grübler, of Leipzig.

2. The sections should be spread out in the stain and should not lie upon each other, as the fluid is then likely to stain unevenly. Large amounts of stain in large dishes should be employed. It is also an advantage to carefully move the sections to and fro.

3. The time required for staining varies, as a rule being less in old, well-ripened stains than in others freshly prepared. This depends also upon the proper hardening and fixation of the tissue and also upon its age. Fresh tissues will stain more deeply and more quickly than old ones.

4. The staining of refractory tissues may be assisted by:

   (*a*) Concentration of the stain.

   (*b*) Staining for a longer time, up to twenty-four hours.

   (*c*) Heating up to 37° C.

(*d*) Adding mordants, as acids and alkalis, anilin oil, etc.

5. The sections should be carefully washed in water to remove all traces of the decolorizing agents used.

6. Sections should be thoroughly dehydrated before being mounted; otherwise those areas containing water will not be transparent and will contain what appear to be oval pigment particles.

Method of staining and mounting sections.

1. Stain.
2. Wash, usually in distilled water.
3. Alcohol (80 per cent.) two to three minutes.
4. Alcohol (95 per cent.) three to five minutes.
5. Alsolute alcohol two to three minutes.
6. Clearing fluid until the specimen sinks below the surface, two to three minutes.
7. Place section on slide, blot off the excess of clearing fluid, and mount in balsam, using a cover-glass.

NUCLEAR STAINS

Aqueous Alum Hematoxylin Solution.—

Hematoxylin crystals....................	1 gm.
Sat. aq. sol. ammonia alum................	100 c.c.
Water..................................	300 c.c.
Thymol.................................	a crystal.

Dissolve the hematoxylin in a little water by the aid of heat. After the solutions have been mixed, expose to the light and air in an unstoppered bottle for about ten days. Then tightly cork.

Delafield's Hematoxylin.—

Hematoxylin crystals......................	4 gm.
Alcohol (95 per cent.)......................	25 c.c.
Sat. aq. sol. ammonia alum.................	400 "

Dissolve the hematoxylin in the alcohol, then add the alum solution. Expose the mixture to the air and light four to five days. Then filter and add:

Glycerin.................................	100 c.c.
Alcohol (95 per cent.)......................	100 "

Expose to light and air for a couple of weeks, then filter and

keep tightly corked. The solution lasts well and stains the more rapidly the older it gets.

Ehrlich's Acid Hematoxylin.—

Hematoxylin crystals	2 gm.	
Absolute alcohol	60 c.c.	
Glycerin	60 "	saturated with ammonia alum.
Water	60 "	
Glacial acetic acid	3 "	

The solution is ripened in an uncorked bottle until it becomes deep red in color; requires a couple of weeks. If kept in well-stoppered bottle precipitates do not form and the solution retains its staining powers for years. Also does not overstain.

Mayer's Hematein.—When hematein is used, ripening is unnecessary, but the results from such stains are not as satisfactory as when hematoxylin is used:

Hematein	0.4 gm.
(Dissolve in a few drops of glycerin.)	
Alum	5.0 "
Glycerin	30.0 c.c.
Water	70.0 "

Hematoxylin Staining.—The nuclei are stained blue. The older the solutions, the quicker they act and the deeper they stain. If the sections are overstained, the excess of color can be removed by placing them in hydrochloric acid alcohol until the proper color is obtained. The acid causes the blue to change to a brown, but the color is regained when the sections are placed in water. The acid should be thoroughly washed out; this can be hastened by using water to which an equal amount of a saturated watery solution of lithium carbonate has been added.

1. Stain three to ten minutes, according to age of stain.
2. Wash thoroughly.
3. Differentiate with acid alcohol, about thirty seconds if sections are overstained.
4. Wash thoroughly.
5. A counterstain, eosin, is usually employed.
6. Dehydrate, clear, and mount in balsam.

Alum Carmin.—

Carmin....................................	1 gm.
Alum solution (5 per cent.).................	100 c.c.

Boil for one-half to one hour and when cool filter. It stains the nuclei a violet red. There is no danger of overstaining and the color is not very easily removed in water or weak acid solutions. This preparation does not work well with objects that are difficult to stain.

The sections are placed:

1. In the stain for ten minutes to two hours.
2. Then washed thoroughly in distilled water.
3. Dehydrated in alcohol, cleared, and mounted.

Lithium Carmin.—

Carmin..........................	2.5 to 5.0 gm.
Sat. sol. lithium carbonate.........	100.0 c.c.

Heat and filter. The nuclei are stained an intense red. Is well adapted for tissues that stain with difficulty. Any excess of color can be removed in acid alcohol. Is a good counterstain for tissues that have been injected with blue substances.

Sections are placed:

1. In the stain for two to three minutes.
2. Washed in water.
3. Differentiated for one-half to one minute in acid alcohol; hydrochloric acid, 1; 70 per cent. alcohol, 100.
4. Washed thoroughly so as to remove the acid.
5. Dehydrated in alcohol, cleared, and mounted in balsam.

Picrolithium Carmin.—

Lithium carmin solution.....................	1 part
Sat. watery sol. picric acid..................	2 parts

Sections are

1. Stained three to five minutes.
2. Washed.
3. Differentiated two to three minutes acid alcohol.
4. Washed thoroughly.
5. Dehydrated in alcohol that has had a little picric acid added to it.
7. Cleared and mounted.

Nuclei are stained brownish red, and the protoplasm yellow.

Borax Carmin.—

Carmin	0.5 gm.
Borax	2.0 "
Distilled water	100.0 c.c.

Mix and heat until boiling begins; should be stirred constantly; then add 4.5 parts of dilute acetic acid (0.5 per cent.) and let stand twenty-four hours; then filter.

This gives the same results as the lithium carmin except that the color is not intense.

Sections placed:

1. In stain for five to fifteen minutes.
2. Washed in water.
3. Differentiated one-half to one minute in acid alcohol solution.
4. Washed in water thoroughly to remove acid.
5. Dehydrated, cleared, and mounted.

Bismarck Brown.—

Either a 3 to 4 per cent. watery solution obtained by boiling and filtering.

Or a concentrated alcoholic solution made in 40 per cent. alcohol, equal to 1½ to 2 per cent.

Sections are:

1. Stained five minutes.
2. Washed in alcohol or 1 per cent. hydrochloric acid alcohol.
3. Dehydrated, cleared, and mounted.

The nuclei are stained a deep brown; the protoplasm, a lighter color. Bacteria are an intense brown. Cannot overstain. This method is especially adapted for micro-photographic work.

Gentian-violet.—Either a 1 per cent. watery or a 2 per cent. alcoholic solution may be used. Are likely to overstain.

Sections are:

1. Stained three to five minutes.
2. Washed in alcohol until they become a pale blue.
3. Then in absolute alcohol.
4. Cleared and mounted.

The nuclear staining is clearer if the sections are put for fifteen to thirty seconds in a 0.5 per cent. solution of acetic acid and then into the alcohol.

Safranin is usually employed after fixing in Flemming's solution to bring out karyokinetic figures.

Sections:

1. Stained one-half to twenty-four hours in a 1 per cent. watery solution of safranin.
2. Quickly washed in water.
3. Washed in absolute alcohol to which 5 to 10 drops of 1 per cent. hydrochloric acid alcohol have been added.
4. Washed in pure absolute alcohol until the section is a clear brown.
5. Cleared and mounted in alcohol.

The resting nuclei are pink, those undergoing mitotic changes are deep red.

Another method is:

Anilin oil	2 c.c.
Water	100 "
Safranin in excess.	

Heat to 60° C. and filter. The solution will last about two months. This forms stains almost immediately. The after-steps are as above.

DIFFUSE AND DOUBLE STAINING

Double staining is employed for the purpose of obtaining a contrast between the nuclei and the plasms and interstitial substance. The nuclear stain is employed first, as the contrast stain is weaker and colors the tissues more diffusely.

Neutral Carmin.—

Carmin powder	5 gm.
Aq. ammon. fort	1 c.c.

These rubbed together, then add:

Distilled water	200 c.c.

Boil until the ammonia is driven off. Allow the solution to stand uncorked for about a week, then filter. The solution works better as it becomes older.

To prepare the stain for immediate use add just enough ammonia to the carmin to make a paste. This should be thinly spread on the sides of the mortar and allowed to dry. Pulverize again, let it remain exposed to the air for twenty-four hours, then dissolve in cold water; it is then ready for use.

To stain sections: Add the stock solution to distilled water until a clear pale red color results. The sections remain in this until they become plainly red, up to twelve hours. The best results are obtained by staining for a long time in a weak solution. Strong solutions stain more rapidly. Wash thoroughly in water, dehydrate, clear, and mount.

The counterstain best used is hematoxylin, and it should be employed first.

Eosin.—Either the form soluble in water, which is the better, or that in alcohol may be used. A few drops of a concentrated solution of either variety is added to a small dish of water and the sections stained until they are of a reddish color—one to three minutes.

Then washed in water.

Dehydrated in alcohol. Should be careful not to leave in the alcohol too long, as it gradually dissolves out the stain.

Cleared and mounted.

This method is preceded by staining in hematoxylin. In such cases the nuclei are blue. In specimens fixed in formalin or sublime solutions the red blood-cells stain a bright red or copper color and the blood-vessels are prominent. Eosinophile cells show up plainly. The other tissues show a diffuse reddish tinge.

Picric acid is generally used in combination with some other stain, as in Van Gieson's method. As the picric acid decolorizes the sections, they should be overstained in the hematoxylin. If iron hematoxylin is used instead of Delafield's, the decolorization does not occur to the same extent.

Van Gieson's method for nervous tissue:

Aqueous sol. acid fuchsin (1 per cent.)	15 c.c.
Sat. aq. sol. picric acid	50 "
Water	50 "

For connective tissue:

Aq. sol. acid fuchsin (1 per cent.)	5 c.c.
Sat. aq. sol. picric acid	100 "

Sections are:

1. Overstained in Delafield's hematoxylin.
2. Washed thoroughly in water.
3. Stained in Van Gieson solution three to five minutes.
4. Washed in water one-half minute.
5. Dehydrated, cleared, and mounted.

Nuclei are stained brownish red; connective tissue, varying shades of light red; axis-cylinders, brownish red; myelin sheaths, yellow; neuroglia and sclerosed fibers, red; amyloid, rose or reddish brown; hyaline, red; colloid, orange or red.

CONNECTIVE TISSUE STAINS

Van Gieson's stain, as already given, may be used. The best results are obtained after fixation in chrome salts or sublimate solutions; are not so good after alcohol.

Mallory's anilin blue stain gives good results after fixation in Zenker's fluid or sublimate solutions. The fibrillæ and reticulum of connective tissue, amyloid, mucous, and other hyaline substances stain blue; the connective tissue can be differentiated from the other substances by their form. Nuclei, protoplasm, fibroglia, fibrils, axis-cylinders, neuroglia fibers, and fibrin stain red; erythrocytes and myelin sheaths, yellow; elastic fibers, pale pink or yellow.

Sections are:

1. Stained in a 0.1 per cent. aqueous solution of acid fuchsin five or more minutes.
2. Transfer to the following solution and stain twenty minutes or more:

Anilin blue soluble in water (Grübler)	0.5 gm.
Orange G. (Grübler)	2.0 "
Aqueous solution of phosphomolybdic acid (1 per cent.)	100.0 c.c.

3. Wash and dehydrate in several changes of 95 per cent. alcohol.

4. Clear in xylol or in oil of origanum (Cretici).
5. Balsam.

ELASTIC FIBER STAIN

Weigert's Stain for Elastic Fibers.—It is best to buy the stain already made up, as its preparation is rather difficult.

The sections are:

1. Stained in the above solution for twenty minutes to one hour.
2. Washed off in alcohol.
3. Blotted with filter-paper, xylol added, and blotted two or three times until the section is clear.
4. Mounted in balsam.

The elastic fibers are dark blue, almost black.

Unna's Orcein Stain.—

Orcein	1 gm.
Hydrochloric acid	1 c.c.
Absolute alcohol	100 "

Sections are:

1. Stained six to twenty-four hours.
2. Washed thoroughly in 70 per cent. alcohol.
3. Washed in water to get rid of the acid.
4. Dehydrated, cleared, and mounted.

The elastic fibers are a deep silky brown color; connective tissue, a pale brown. This method has the advantage that elastic fibers that have degenerated into elacin take the basic blue stain.

Levaditi Stain for Treponema Pallidum.—

1. Fix small pieces of tissue, 1 to 2 mm. thick, in 10 per cent. formol for twenty-four hours.
2. Wash in water a few minutes; place in 95 per cent. alcohol for twenty-four hours.
3. Wash in distilled water until the tissue sinks.
4. Place in a 2 per cent. solution of silver nitrate and put in an incubator at 38° C. for three to five days. It is best to use amber-colored bottles.
5. Wash briefly in distilled water, then put in the following solution for twenty-four to forty-eight hours at room-temperature:

Pyrogallic acid	3 gm.
Formalin	5 c.c.
Aq. dest	100 "

6. Wash in water, dehydrate, and embed in paraffin. The treponema will stain black; the rest of the tissue, yellow.

Kaiserling's Method of Preserving Natural Colors in Tissues.—

1. Fixation for one to five days in—

Formaldehyd	200 c.c.
Water	1000 c.c.
Nitrate of potassium	15 gm.
Acetate of potassium	30 "

Change the position of the specimen frequently. The time of fixation varies with the tissue or organ and the size of the specimen.

2. Drain and place in 80 per cent. alcohol one to six hours, and then in 95 per cent. alcohol for one to two hours, to restore the color.
3. Preserve in—

Acetate of potassium	200 gm.
Glycerin	400 c.c.
Water	2000 "

Exposure to light gradually affects the colors.

BLOOD STAINING

Before being stained the blood must be fixed to the slide either by heat or by some chemical.

Heat may be used in all cases except when Wright's stain is employed; it must be used with Ehrlich's triple stain to get good results. The films should be exposed to a dry heat of from 100° to 110° C. for ten to fifteen minutes.

Chemicals.—The smears are fixed in absolute alcohol or ether or a mixture of equal parts of the two for five to ten minutes. Then dried and stained.

Stains.—*Wright's.*—It is best to procure this stain ready made. It is employed as follows, as no previous fixing is necessary:

The unfixed film is covered with the solution and stained for

a minute. Distilled water is added drop by drop until a metallic scum appears on the surface of the fluid and is allowed to remain two to three minutes. Then wash the film, which is a deep blue or purplish color, until it becomes yellowish or pink. Dry between blotting-paper and mount in balsam.

The erythrocytes will be stained orange or pink; the nuclei of the leukocytes, blue; neutrophile granules, lilac; eosinophile granules, pink; fine basophile granules, deep blue; coarse mast-cell granules, deep purple. The malarial organism stains blue.

Ehrlich's Triacid.—Best bought ready made.

After fixing with heat, stain five to eight minutes; wash in running water, dry, and mount.

Erythrocytes stain orange; nuclei of the leukocytes, greenish blue; neutrophile granules, violet or lavender; eosinophile granules, copper red; basophile granules are unstained.

Polychrome methylene-blue (Goldhorn's) is bought ready made.

After fixation for fifteen to twenty seconds in methyl-alcohol, wash in water and, without drying, stain for one to two minutes. Wash thoroughly in running water, dry with blotting-paper, and mount.

This method shows very well granular degenerations of the erythrocytes, the nuclei of erythroblasts and leukocytes, basophilic granules, and most bacteria. It is a very good stain for the malarial organism. If the film is first stained for ten to fifteen seconds in a 0.1 per cent. aqueous solution of eosin, washed, and then the methylene-blue used, a very good picture of the acid-coloring elements is given.

Eosin and Methylene-blue.—Fix the smear in absolute alcohol alone or mixed with an equal quantity of ether. Stain in a 0.5 per cent. solution of eosin in absolute alcohol, to which an equal quantity of water is added, for about five minutes without heating. Wash and dry, then counterstain in a saturated aqueous solution of methylene-blue for about one minute. Wash again, dry, and mount.

Gives a good picture of the nuclei of the basophilic granules and of the malarial organism: eosinophile granules stain red; the protoplasm of the polymorphonuclear leukocytes colors a slight pink; the granules remaining unstained.

CHAPTER XVII

BACTERIOLOGIC METHODS

CULTURE-MEDIA

As has already been stated (p. 21), there are certain requirements known as Koch's laws, or postulates, that must be fulfilled in order that we can prove a certain organism to be the cause of a definite pathologic condition. These require, among other things, that the organism be grown outside of the body on artificial culture-media; these to be composed of such substances in such proportion as will enable the bacteria to live and multiply. Inasmuch as the different bacteria vary greatly in their metabolic activities, it becomes necessary to have various kinds of media; there are, however, certain forms that are employed routinely. Such media should contain at least 80 per cent. of water, should be of neutral or feebly alkaline reaction, and of a composition which, for the pathogenic types at least, should closely approximate the juices of the animal body. Such nutritive materials may be either liquid or solid, and some of the most useful may be liquefied and solidified at will.

Bouillon.—This medium is used by itself and also as the nutritive basis of certain solid media. It may be made up with lean beef or with 3 gm. of beef extract. If the former is used it must be freed from fat and gristle and finely minced; 500 gm. of it are mixed with 1000 c.c. of water and allowed to stand on ice for twelve hours. At the end of this time the liquor is poured off, that remaining in the meat squeezed through a cloth, and enough water added to bring the amount up to 1000 c.c. It is then filtered, and to the clear filtrate is added 10 gm. of Witte's peptone, 5 gm. of sodium chlorid, and enough water to bring the quantity up to 1000 c.c. This mixture is boiled until everything is dissolved, and it is then neutralized, as its reaction is very acid.

The neutralization should be very carefully carried out so that the final reaction is slightly alkaline. This is done by carefully adding a 10 per cent. solution of caustic soda and testing with litmus-paper. During this process the solution is kept boiling. After the materials are all dissolved and the solution titrated, it should be allowed to cool before filtering. If filtered while hot there will be a subsequent precipitation of meat-salts, which will cloud it.

Glucose bouillon is similar to the above, except that it contains 1 per cent. glucose in addition.

Agar-agar.—To 1000 c.c. of beef bouillon 15 gm. of agar-agar are added and boiled for one hour, constantly stirring. Water is added at various intervals to keep up the required volume. After the boiling is done the contents are allowed to cool to 60° C., at which point an egg is beaten into the fluid, which is again boiled for about ten minutes. Then filter while hot through wet filter-paper. A jacketed filter kept warm by a gas flame facilitates the process. As the fluid cools while filtering, it has to be again heated until all passes through. The finished agar should be a colorless, nearly transparent, firm jelly.

The purpose of the agar-agar is to give a medium that will remain solid at a temperature equal to that of the body, which is the best for many bacteria, the agar itself not contributing any nourishment to the medium. The agar will melt at about 42° C., but will again solidify when cooled.

Gelatin.—To 1000 c.c. of boiling beef bouillon add 100 gm. of golden seal French gelatin. When the gelatin is thoroughly dissolved boil for about five minutes and neutralize by the method described for bouillon. The mixture is cooled to 60° C., an egg beaten in, boiled about ten minutes, and filtered through wet filter-paper. Sufficient water should be added to bring the quantity up to the original amount. It may have to be reheated a couple of times before filtration is complete. As the gelatin solution is strongly acid in reaction, it must be corrected carefully by titration. Care must be taken not to bring the mixture to the boiling temperature more frequently than is necessary, as the power of coagulation may be destroyed.

This medium melts at temperatures above 22° C.

Glucose gelatin is gelatin that has been dissolved in glucose bouillon.

Blood-serum (*Löffler's Mixture*).—The blood-serum is obtained by collecting it at a slaughter-house. Jars holding about 1 gallon should be used. These should be clean and sterile. The collected blood is put aside in a cool place for twenty-four to forty-eight hours until the blood is completely clotted. If the clot adheres to the side of the jar, loosen it with a glass rod. The clear serum is removed with a pipet. This is then mixed with glucose bouillon.

Glucose bouillon (1 per cent.)................	1 part
Beef blood-serum..........................	3 parts

The above is then run into test-tubes to a depth of about 4 cm. These are placed on an incline so that they will be on a slant when coagulated. In this position they are placed in a hot-air sterilizer and kept at a temperature between 85° and 90° C. for one hour. The thermostat should be carefully watched so as not to have the heat vary from the above figures. After the medium has become thoroughly coagulated the tubes are sterilized in steam for one-half hour on three successive days. When blood-serum tubes are not available a good substitute in the form of a hard-boiled egg may be used. Remove the egg from the water, and with a sterile instrument remove a part of the shell, leaving the coagulated albumen exposed. Inoculate this surface with the suspected material, cover with a glass, and then place near a stove or in a "Thermos" bottle, and allow to incubate for eighteen to twenty-four hours. The blood-serum is particularly useful in the cultivation of the Bacillus diphtheriæ, which grows upon it rapidly and with a characteristic appearance.

Litmus Milk.—To milk that has been freed from cream enough of a freshly prepared aqueous solution of litmus is added to give it a blue color. This is run into test-tubes which are treated by intermittent steam sterilization. Fresh milk should be used and the process quickly carried out to prevent as much as possible the growth of bacteria. This medium is the best for determining the formation of acids or alkalis by bacteria.

Potato Cultures.—The potatoes should be thoroughly scrubbed with brush and water. Solid cylinders of a size to fit the test-tubes are cut with a cork-borer. They are then split obliquely and the pieces placed in running water for some twelve hours. The oblique pieces are then placed in test-tubes with the larger end downward. A few drops of water should be added to prevent drying. The tubes are then put through the fractional steam sterilization.

Dunham's Peptone Solution.—

Peptone	10 gm.
Sodium chlorid	5 "
Distilled water	1000 c.c.

The peptone and sodium chlorid are dissolved by boiling and the mixture filtered. Test-tubes are filled and sterilized. This solution is commonly employed for the detection of indol.

Filling of Test-tubes.—New test-tubes are best cleaned by washing in a very weak solution of nitric acid, then rinsing in water, and allowing to become dry or nearly so. Old tubes that have contained cultures are boiled for nearly one hour in a 6 per cent. solution of common soda.

The cleaned tubes are plugged with *raw* cotton and placed in the hot-air sterilizer at 150° C. until the cotton has turned brownish. This is to mold the stopper to the shape of the tube.

To fill the tubes it is best to take a large funnel and by means of a short piece of rubber connect it to a piece of glass tubing a couple of inches in length. The supply of the medium is controlled by a pinch-cock on the rubber. The glass tube is inserted into the test-tube, the required amount of medium run in, and the cotton plug put back. Care should be taken not to get any of the culture-medium on the neck of the tube, as the cotton would stick to it. If "slant" cultures are to be made, run in about 5 c.c. of fluid; if "stab" cultures, about 8 to 10 c.c. should be used. The filled tubes are then sterilized. After the final sterilization, if "slant" cultures are to be made, the test-tubes are so placed that the medium will come about half-way up the side of the tube.

Instead of test-tubes, flasks of varying sizes may be used to contain the medium.

Sterilization of Culture Media.—This may be done by the intermittent method. In this the media are exposed to steam on three successive days for a period of thirty to forty-five minutes. A single sterilization will kill all bacteria except those that are in the spore stage. These bodies will, however, develop within the twenty-four hours into the adult form, and are then killed by the subsequent sterilization.

Instead of the above the autoclave may be used. It is a metal chamber so arranged as to allow sterilization under pressure. A temperature of 110° C. is obtained, and in it all bacteria and spores are destroyed in twenty to thirty minutes.

After the final sterilization if "slant" cultures are to be made the test-tubes are so placed that the medium will come about half-way up the side of the tube.

When the media have solidified the tubes can be kept a longer time if the cotton is trimmed off and rubber caps put on.

Sterilization of Apparatus.—Metal bodies that will not be injured, platinum wires, forceps, etc., may be placed directly in the flame of a Bunsen burner. Glassware is sterilized by hot air, by steam, or by boiling. Chemical sterilization is not often employed.

Varieties of Cultures.—

1. Slant.
2. Stab.
3. Petri dish.
4. Esmarch tube.
5. Hanging drop.
6. Anaërobic.

1. *Slant Cultures.*—A platinum wire is taken and heated in the flame. When cool it is inserted into the material to be examined. Then, without touching anything, not even the sides of the tube, the point of the wire is carefully drawn over the surface of the medium and the wire again sterilized. When the cotton plug is removed, the end of the tube should be passed through the flame. Care should be taken at all times that the platinum wire is carefully sterilized before being laid anywhere.

2. *Stab cultures* are made by carefully inserting the platinum

wire, which should be straight, into the center of the culture-media. The same precautions as mentioned above should be observed.

3. The *Petri dish* consists of a shallow glass dish with a cover. It is used to a large extent for the purpose of isolating colonies and obtaining pure growths. The tubes inoculated directly from the material examined usually contain several varieties of organisms. The method of *isolating* is as follows: Three tubes of agar-agar or gelatin are melted and then placed in a water-bath at a temperature between 40° and 42° C. A platinum wire with a small loop at the end is inserted into the infected substance and then a tube is inoculated. From this tube a loopful is carried over to tube No. 2, and a third tube is inoculated from the second, the platinum wire being sterilized each time. Three sterile Petri dishes are taken and a tube is inserted under the cover of one and its contents poured out. This is done with all three, care being taken to have the medium evenly distributed over the bottom of the dish. They are then incubated twenty-four hours at a temperature of 37° C.

The first tube will contain so many organisms that Petri dish No. 1 will be covered with colonies. The second tube, being diluted, will give fewer colonies on dish No. 2, while dish No. 3, obtained by pouring out tube No. 3, will have only a few scattered colonies. From this last dish the individual growths may be removed with a sterilized platinum needle and inoculated into a fresh tube, a pure culture thus being obtained.

4. The *Esmarch tube* is made by taking an inoculated tube of melted agar or gelatin, laying it on a block of ice, and rotating till the medium is distributed in a thin coat on the inside. Care must be taken that the contents do not come in contact with the cotton plug. This method has been practically supplanted by the Petri dishes.

5. *Hanging-drop cultures* are obtained by taking a slide in which there is a depression and a ring of vaselin is made around it. A sterilized cover-glass is taken, a drop of bouillon placed on it, and this is inoculated with the usual precautions. The cover-glass is inverted over the depression in the slide and

pressed down upon the vaselin. This is put in the incubator for twelve to twenty-four hours and then examined.

6. *Anaërobic cultures* may be obtained in various ways, the essential point being the elimination of free oxygen. A test-tube half full of a medium that will become solid on cooling is boiled, rapidly cooled, and then inoculated by a deep stab. On top of this may be poured melted paraffin, oil, or vaselin to keep out the air. Buchner's method consists in the use of two tubes, a small one to contain the culture, and a larger one to contain a fluid that will absorb the atmospheric oxygen. The solution used consists of pyrogallic acid and sodium hydroxid, about 2 gm. of the former, 20 c.c. of a 10 per cent. solution of

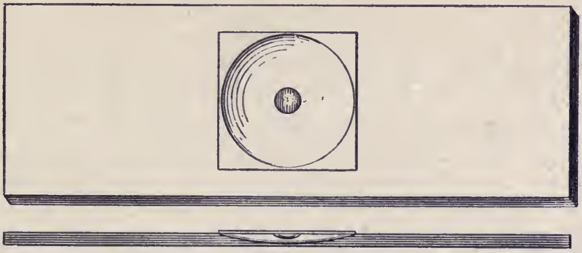

FIG. 126.—THE "HANGING DROP" SEEN FROM ABOVE AND IN PROFILE (McFarland).

the latter. This is poured into the larger tube, the smaller one placed within it, and it is then tightly corked. A simpler method is one in which a larger tube containing a liquid medium is used. Into this is placed a smaller tube with the closed end uppermost. During sterilization the air will be displaced, and when the liquid cools the smaller tube will be full of the medium. In this the anaërobic organisms will grow. This method is also of value in determining whether there is any gas formation, and may be used in place of Smith's fermentation tubes.

The oxygen within the container may be replaced by an atmosphere of hydrogen, and the latter tightly sealed.

EXAMINING BACTERIA

Although the greater part of the examination of micro-organisms is done with stained specimens, yet they should

always be examined in the unstained and living condition as well. The best way to do this is by means of the *hanging drop*. In this method a slide with a concavity is used. Around this depression a ring of vaselin is made. A drop of the material to be examined is placed in the center of a clean cover-glass, which is then inverted over the depression in the slide and is pressed down upon the vaselin. Care should be taken that the drop is not large enough to touch the slide. The edge of the drop should be examined, as the central portion is too thick. By this method can be determined the shape, size, grouping, division, sporulation, and motility of the organism.

STAINING BACTERIA

Staining Cover-glass Preparations.—A well-cleaned cover-glass or slide has a small portion of the material for examination spread out on it in a very thin layer by means of a sterilized platinum wire. The preparation is allowed to dry; it is best not to do it over a flame. When dry the cover-glass is passed rather slowly three times through the flame of a Bunsen burner. This coagulates the albumin and prevents the material being washed off during the process of staining. The cover-glass is covered with the stain and gently warmed for fifteen to twenty seconds over a small flame. The specimen is then washed in water, dried by blotting and by gently warming, and mounted in balsam.

Various of the anilin colors are the ones chiefly used in bacterial staining. They may be used alone or in combination with certain reagents employed to increase the staining power.

Saturated alcoholic solutions of the stains should be kept in stock, and from them the dilute aqueous solutions can be prepared. These latter, however, do not keep well, so various standard preparations are usually kept on hand.

Löffler's Methylene-blue.—

Sat. alc. sol. methylene-blue................	30 c.c.
Caustic potash in water (1:10,000)..........	100 "

This keeps a long time and stains rapidly.

Neisser's Stain for Diphtheria.—

Solution No. 1

Methylene-blue	0.1 gm.
Alcohol	2.0 c.c.
Glacial acetic acid	5.0 "
Distilled water	95.0 "

Dissolve the methylene-blue in the alcohol and add it to the acetic-acid-water mixture. Filter.

Solution No. 2

Bismarck brown	0.2 gm.
Water (boiling)	100.0 c.c.

Dissolve the stain in the boiling water. Filter. To stain: Fix the preparation. Pour on the acetic-acid-methylene-blue solution and allow to act from thirty to sixty seconds. Wash. Then pour on the Bismarck-brown solution, and after thirty seconds wash off with water. Dry and mount. The bodies of the bacilli are brown, with dark blue spots at either end. Best results are obtained with cultures from nine to eighteen hours old.

Carbol-thionin.—

Sat. sol. thionin in 50 per cent. alcohol	10 c.c.
Carbolic acid aq. sol. (2 per cent.)	100 "

Carbolfuchsin.—

Sat. alc. sol. fuchsin	10 c.c.
Watery sol. carbolic acid (5 per cent.)	90 "

This stain is very permanent and is useful for many purposes. It is employed in the differential diagnosis of tubercle bacilli.

The following method, that of Ziehl-Nielson, is commonly employed for staining tubercle bacilli, particularly in sputum. After having made, dried, and fixed the smear, the cover-glass or slide is covered with carbolfuchsin and carefully heated, until steam rises, for some three or more minutes. Care must be taken not to boil the stain and to replace the solution as it evaporates. Then wash the smear thoroughly in water and decolorize with about a 10 to 15 per cent. solution of nitric acid in 95 per cent. alcohol. Will take about thirty seconds

to a minute. Wash again in water and counterstain in Löffler's methylene-blue. Wash and examine. The tubercle bacilli will appear as minute red rods; all other organisms and cells will be blue.

With Gram's method the bacillus retains the stain.

Anilin Gentian-violet.—

Sat. alc. sol. gentian-violet	16 c.c.
Anilin water	84 "

Anilin water is made by taking:

Anilin oil	5 c.c.
Distilled water	95 "

Shake thoroughly until a milky fluid is obtained; then filter.

This stain should be freshly prepared when needed, as it does not last more than ten days.

Carbol Gentian-violet.—

Sat. alc. sol. gentian-violet	1 c.c.
Aq. sol. carbolic acid (5 per cent.)	10 "

This solution is permanent, but tends to overstain.

Gram's Method.—After the cover-glass has been smeared and fixed it is stained in:

1. Anilin or carbol gentian-violet thirty seconds.
2. Washed in water two or three seconds.
3. Put in Gram's solution, as follows, for thirty seconds:

Iodin	1 gm.
Potassium iodid	2 c.c.
Water	300 "

4. Washed in 95 per cent. alcohol until the color ceases to come out of the preparation.
5. Dry by blotting and in air and mount in balsam.

The value of this method lies in the fact that certain bacteria will retain the stain, while others give it up. In those organisms retaining the stain there has been a combination of mycoprotein, anilin dye, and the iodids that forms a compound insoluble in alcohol. The bacteria stain dark blue or black while the nuclei are only faintly colored. Nuclei that are undergoing division may stain rather deeply.

An organism is said to stain by Gram's method when it is not decolorized. This power is made use of to differentiate certain organisms that may resemble each other in size and shape.

The more important pathogenic bacteria are divided as follows, according to their reaction to Gram's:

Stained by Gram's Method	Decolorized by Gram's Method
Staphylococcus pyogenes.	Gonococcus.
Streptococcus pyogenes.	Bacillus typhosus.
Streptococcus capsulatus.	B. coli communis.
Actinomycosis.	B. of malignant edema.
Bacillus anthracis.	Spirillum of Asiatic cholera.
Pneumococcus.	Diplococcus intracellularis meningitidis.
B. diphtheriæ.	B. pyocyaneus.
B. lepræ.	B. of influenza.
B. tuberculosis.	B. of dysentery.
B. tetanus.	B. of bubonic plague.
B. aërogenes capsulatus.	B. of glanders.
	Spirochæta of relapsing fever.

METHODS FOR STAINING SPORES

Spores are the resting forms of various organisms and are stained with difficulty, but when once stained are hard to decolorize.

Abbott's Method.—

1. Stain the cover-glass deeply with methylene-blue, heating until the solution boils.
2. Wash in water.
3. Wash in 95 per cent. alcohol, containing 0.2 to 0.3 per cent. HCl.
4. Wash in water.
5. Stain for eight to ten seconds in anilin-fuchsin solution.
6. Wash in water, dry, and mount.

The spores are stained blue; the bodies of the bacteria, red.

Möller's Method.—

1. Wash the cover-glass for two minutes in chloroform.
2. Wash in water.
3. Place in a 5 per cent. watery solution of chromic acid for one-half to two minutes.

4. Wash in water.
5. Stain with carbolfuchsin for one minute, heating the solution slowly until it boils.
6. Thoroughly decolorize in a 5 per cent. solution of sulphuric acid.
7. Wash in water.
8. Stain in aqueous methylene-blue (1 gm. to 100 c.c.) for thirty seconds.
9. Wash in water, dry, and mount.

The spores will be red; the bacteria, blue.

The most satisfactory spore-staining method is really the negative staining of the spore obtained when a bacterial preparation is stained by dilute carbolfuchsin or Löffler's methylene-blue. The spore appears as a highly refractile piece of glass in a colored frame. The acid-fast method, as for tubercle bacilli, gives good results, but the decolorizing must be lightly done, otherwise the spore will lose its red stain.

STAINING OF FLAGELLA

Löffler's Method.—

1. Flood the cover-glass with the following solution, which should be filtered before using:

Aqueous solution of tannic acid (20 per cent.)	10 c.c.
Cold saturated solution of ferrous sulphate....	5 "
Saturated aqueous or alcoholic solution of gentian-violet or fuchsin....................	1 "

   This is very gently heated, not boiled, for about one minute.

2. Wash in water.
3. Stain in anilin gentian-violet or anilin-fuchsin with gentle heating thirty to sixty seconds.
4. Wash, dry, and mount.

Bowhill's Method.—Stain the cover-glass in the following solution, heating gently for ten to fifteen minutes:

Saturated alcoholic solution of orcein.........	10 c.c.
Aqueous solution of tannin (20:80)..........	10 "
Distilled water............................	30 "

Filter the mixture before using. The orcein stain should be at least nearly two weeks old.

In **staining sections** for bacteria Gram's method or that used for the tubercle bacillus is generally employed. Better results are obtained with paraffin sections, but celloidin may be used.

Staining Capsules.—

1. Cover the preparation with glacial acetic acid for a few seconds.
2. Drain off (do not wash) and replace with anilin gentian-violet. Pour this off and add more stain until all of the acid has been removed.
3. Wash in a 2 per cent. solution of sodium chlorid and examine in the same.

PART II—SPECIAL PATHOLOGY

CHAPTER XVIII

THE BLOOD

Blood is composed of two parts, the *cellular* elements, and the fluid, *plasma* or *liquor sanguinis*. Although its *reaction* to litmus is alkaline, the use of more delicate reagents would indicate that the blood may be considered as approximately a neutral fluid. Its *specific gravity* varies between 1055 and 1065, the average being 1060. The *odor* is characteristic in different animals. The *color* is due to the presence in the erythrocytes of an iron-containing albuminous substance, hemoglobin, which has a marked affinity for oxygen and other gases. *Arterial* blood is freshly aërated and is bright red in color, *venous* blood is bluish. The variations in color depend upon the relative proportions of oxygen and carbon dioxid in the two varieties of blood.

The chief gaseous constituents and their proportions are as follows:

	Arterial	Venous
Oxygen	21.6	6.8
Carbon dioxid	40.3	48.0
Nitrogen	1.8	1.8

Coagulation.—On standing, except under certain conditions, the blood will tend to separate into its two portions, the cellular elements and the plasma. In a short time, the period varying according to the composition of the blood, the phenomenon of coagulation will occur. In this process the plasma changes into serum and the clot, this latter being composed of minute threads of fibrin which hold the corpuscles in a network. In normal blood a substance called fibrinogen is present in the plasma. Under the action of the ferment

thrombase, which is present as prothrombase in the leukocytes, the fibrinogen is converted into fibrin. The prothrombase is changed into thrombase by the action of calcium compounds, which appear to be the active agents in causing coagulation.

Normally coagulation should take place in from three to eight minutes, but it may vary considerably under pathologic conditions.

Hemoglobin.—The color of the blood is due to the combination of oxygen and hemoglobin, the latter owing its ability to take up oxygen to the presence of iron in the molecule. The amount of the coloring matter may be much diminished either by a decrease in the actual number of red cells, or by each cell containing less than its normal amount.

Under certain conditions the hemoglobin may be dissolved out of the cells and escape into the plasma, *hemoglobinemia*. The cells that have lost the coloring matter are sometimes referred to as *shadow corpuscles*.

A diminution in the amount of hemoglobin without a decrease in erythrocytes is known as *oligochromemia*, the individual cells containing less than normal. In some diseases there is an absolute reduction of hemoglobin, but the individual red cells may contain an increased amount, the diminution being due to an actual decrease in the number of erythrocytes.

Methemoglobin is closely related to oxyhemoglobin but differs in that the oxygen in the former is in a more stable combination and cannot be made use of by the tissues. It gives a chocolate color to the blood and occurs in various forms of poisoning as from the chlorates, nitrites, acetanilid, antipyrin, and some others.

In poisoning by carbon monoxid the blood is a bright cherry red in color. In carbon dioxid poisoning the blood is dark in color.

Color-index.—This term is used to indicate the amount of hemoglobin contained in each red cell, as compared with the amount present in a normal erythrocyte. It is obtained by dividing the hemoglobin percentage by the percentage of

red cells. This latter is procured by dividing the number of red cells found in the blood by 5,000,000, the number accepted as normal. This percentage can be gotten readily by multiplying the number of hundred thousands of red cells by two. The color-index is normally one; a hemoglobin value of 100 per cent. is associated with a blood count of 5,000,000 red cells.

In some conditions the amount of hemoglobin is greatly reduced without a corresponding diminution in the amount of reds. In such the index is less than one. This occurs particularly in chloroses and splenic anemia. At other times the diminution of the reds is much greater proportionately than that of the hemoglobin, the color-index will then be high. This is the condition found in the pernicious types of anemia.

Chlorosis

$$\left.\begin{array}{l}\text{Red blood cells } 4{,}000{,}000 \times 2 = 80 \text{ per cent.}\\[1em] \text{Hemoglobin } 40 \text{ per cent.}\end{array}\right\} \begin{array}{l}40 \div 80 = 0.5\\ \text{color-index.}\end{array}$$

Pernicious Anemia

$$\left.\begin{array}{l}\text{Red blood cells } 1{,}000{,}000 \times 2 = 20 \text{ per cent.}\\[1em] \text{Hemoglobin } 20 \text{ per cent.}\end{array}\right\} \begin{array}{l}20 \div 20 = 1.\\ \text{color-index.}\end{array}$$

Erythrocytes.—Are flattened, thin bi-concave discs of an average diameter of 7.2 to 7.8 μ, and are non-nucleated in their normal adult condition. They are very elastic so that they can pass readily through the small capillaries. Their active life is supposed to be quite short, their function is the carrying of oxygen from the lungs to the tissues throughout the body. In abnormal conditions these cells may vary greatly in size, shape and hemoglobin content. *Microcytes* are those averaging 3.5 μ in diameter. These are observed in all severe anemias and as a rule stain deeply and uniformly. *Macrocytes* are those varying from 10 μ to 20 μ. They indicate a severe and chronic anemia, such as pernicious anemia. *Poikilocytes* are those which show marked alteration in shape, usually pear-formed. They may be large or small and when

occurring in large numbers, the condition is known as *poikilocytosis*. It is indicative of severe anemia with degenerative changes in the red cells. At times such cells may be nucleated *poikiloblasts*.

Nucleated red cells are always pathological when found in the circulation with the exception of the first few days following birth. *Normoblasts* are nucleated red cells similar in size, shape and color to the normal cell. The nucleus is about one-third the diameter of the cell, stains densely, is homogeneous, sharply defined and spheroidal in shape, without any definite chromatin network. It is usually situated near the periphery of the cell. At times the nucleus may be protruded partially or even escape entirely from the erythrocyte. Occasionally the nucleus may show indications of multiplication. The presence of these cells in the blood indicates an increased activity of the blood-making organs, especially of the bone-marrow, an attempt at rapid regeneration. They are commonly found in the milder forms of anemia, chlorosis and acute anemia from hemorrhage. In severe types of anemia they are associated with the megaloblasts.

Megaloblasts.—These cells correspond in size with the macrocytes, varying from 9 μ to 20 μ. The cell is usually circular or oval, but may show marked irregularities. The protoplasm appears swollen and shows marked polychromatophilia, is varying in color from yellow to purple. The nucleus is large, varying from 6 μ to 10 μ and may be situated either centrally or peripherally. It varies greatly in shape and in staining, frequently being poorly defined and showing very faint basic staining. Sometimes there may be present mitoses or various stages of karyorrhexis with fragmentation, vacuolation and minute subdivisions of chromatin. Their presence in the blood probably indicates a reversion to an embryonal type of blood formation. They are evidences of a degenerative process of the blood-forming organs. When present as a majority of the nucleated red cells, particularly if the cells are unusually large and the nuclei show unequal mitoses, a diagnosis of primary pernicious anemia can be made.

Microblasts are nucleated red cells of from 2 μ to 5 μ, are not frequently found and do not appear to have any special significance.

Number of red cells may vary greatly and such variations are not uncommon. Normally there is found in a cubic millimeter of blood five million cells in the male and four and a half million in the female. The number may be lowered temporarily in women as a result of menstruation, child-birth and lactation. It also varies somewhat according to the age, being particularly high at birth and a few days after, but soon becomes normal and remains with but little change during health. There is also some increase in number at high altitudes.

Oligocythemia refers to a decrease in the number and is usually associated with a decrease in the total amount of hemoglobin. It may be temporary or permanent, according to the underlying cause, such as acute hemorrhages or in cases of chronic pernicious anemia. In the latter a count as low as 100,000 red cells has been reported.

Polycythemia refers to an increase in the number of red cells. Conditions that cause a great loss of liquid from the body, as in profuse diarrheas, may cause a greater concentration of the blood and an apparent increase in the cells. It may occur in phosphorous poisoning, acute yellow atrophy of the liver, and in some cases of general hepatic insufficiency.

Leukocytes.—These are nucleated blood-cells that do not contain hemoglobin and are known as the white cells. Certain of them are capable of ameboid motion and on account of their ability to surround and take up foreign particles are called phagocytes. They vary in size from 5 μ to 10 μ and from 5000 to 9000 in number to a cubic millimeter.

Although many attempts to classify them have been made, the best method is probably that of Ehrlich in which both the nuclear and granular staining characteristics are made use of.

Polymorphonuclear or *neutrophile* leukocytes constitute the greater number, the percentage varying from 65 to 75. They are about 10 μ in diameter and contain nuclei that vary

greatly in shape. At times the nucleus looks as though it were separated into two or more distinct nuclei, but careful examination shows these masses to be connected by fine threads. The nucleus is strongly basophilic and usually stains a deep blue. In the protoplasm are numerous small granules that stain purple or violet, a neutral reaction to Ehrlich's triple stain. These are the cells that are particularly active and phagocytic. When outside of the blood-vessel they form the usual pus cell.

Eosinophiles.—These are polymorphonuclear leukocytes characterized by the presence in the cytoplasm of large coarse granules that stain very deeply with eosin. The nuclei do not stain very deeply with the nuclear dyes. The average number is from 100 to 200 cells.

Basophiles are polymorphonuclear leukocytes containing rather coarse granules in the cytoplasm that stain with basophilic anilin dyes. Are very seldom found. Are also known as "mast-cells."

Lymphocytes may be large or small. The *small* lymphocyte is about the same size as a red blood-cell and contains a round nucleus, situated either centrally or slightly excentrically, which stains quite deeply. Surrounding the nucleus is a narrow zone of cytoplasm that is free from granules. This type forms about 20 per cent. of the leukocytes. The *large* lymphocyte closely resembles the small, but is larger, 8 to 10 μ, and contains a nucleus that is more oval and which does not stain as deeply as that of the smaller variety. There is also more cytoplasm present. This form constitutes about 2 to 4 per cent. of leukocytes.

Large mononuclear leukocytes (endothelial leukocytes) are usually a little larger than the polymorphonuclear type and each contains an oval excentrically situated nucleus which is usually curved or indented, but never divided. It stains lightly, never intensely like the nucleus of the polymorphonuclear. The cytoplasm contains no granules and is limited by no definite cell membrane. The so-called "transition forms" are cells derived from the same source as the above, but ones in which the nucleus is deeply notched. Most

observers class the large mononuclear cell with the large lymphocyte but others believe that they are derived mainly from the endothelial cells lining the blood-vessels, but also from the lymph vessels, by proliferation and desquamation.

	Percentage	Number per c.c.
Small mononuclears } lymphocytes	20–25	1200–2000
Large mononuclears } lymphocytes	3–5	200–400
Polymorphonuclear neutrophiles	65–75	5000
Polymorphonuclear eosinophiles	2–4	100–200
Polymorphonuclear basophiles	0–½	0–50

Myelocytes are cells derived from the bone-marrow and are never seen in the blood under normal conditions. They may vary in size from that of a red blood-corpuscle to that of a large mononuclear cell. In staining reaction the cytoplasmic granules may be neutrophilic, eosinophilic, or basophilic. The neutrophile is the most common. It contains a large round or oval nucleus that stains poorly and is eccentrically placed, as a rule. These cells are found chiefly in myelogenous leukemia.

Number of Leukocytes.—The various forms of leukocytes may vary greatly in a variety of different conditions and from these variations much information may be obtained. If more than 10,000 per cubic millimeter are present, the condition is considered pathological.

Leukocytosis is the term applied to a temporary increase in the number of polymorphonuclear leukocytes; this may be either physiological or pathological. The former is a temporary condition occurring normally during digestion, in pregnancy and in the newborn. Pathological leukocytosis is seen particularly in inflammatory conditions due to bacterial infection, especially by the pyogenic organisms. In croupous pneumonia the number has gone as high as 100,000 per cubic centimeter. This increase may also be present in malignant disease, following hemorrhages and shortly before death.

Speaking generally, leukocytosis represents the degree of resistance possessed by the body. A high count usually

indicates a strong reaction to the infection, while a low count is indicative of a lessened resistance, or a mild degree of infection. Care must be observed that the two are not confused.

Lymphocytosis refers to an increase in the number of lymphocytes. This occurs in marasmus, syphilis, whooping-cough, in most of the infectious diseases of childhood, and especially in lymphatic leukemia.

Eosinophilia indicates an increase in the number of eosinophiles. This occurs in various diseases of the bone-marrow, particularly myelogenous leukemia. In true bronchial asthma there is a great increase, as there also is in parasitic infections, as by the trichinella. In many skin diseases they are increased, also in gonorrhea and sarcoma.

Leukopenia indicates a diminution in the number of leukocytes below 5,000 and is commonly found in typhoid fever.

Blood plates are small, oval or round, colorless bodies, measuring from 2 to 3.5 μ in diameter, present in the blood plasma in great numbers. They are very viscid, of high specific gravity, and are closely connected with the formation of fibrin. Their origin is not as yet settled, some believing that they are broken down red cells, or extrusions of the nuclear substance of the red cell. Wright holds that they are formed as budding masses from the megakaryocytes, the giant cells of the bone-marrow.

PATHOLOGY OF THE BLOOD

PRIMARY ANEMIA

Primary anemias are those conditions of decreased hemoglobin and red cells in which no demonstrable cause can be found for the blood change.

Chlorosis is a form of anemia occurring mainly in girls at the age of adolescence. It is characterized by a great reduction in the amount of hemoglobin without a corresponding reduction in the number of erythrocytes. The color-index is low, frequently falls to 0.5.

The cause is unknown. Various conditions such as hypoplasia of the arterial system and of the genitalia, intestinal

autointoxication, vasomotor neuroses, heredity, poor hygiene, etc., have been advanced as explanations of the condition. Unsanitary conditions about the age of puberty undoubtedly play an important part.

The blood shows certain characteristic conditions, it is very pale on account of the reduction of the hemoglobin, 40 to 30 per cent. of the normal not being unusual, sometimes it may drop as low as 20 per cent. with a color index of 0.5. The number of red cells is reduced, as a rule not below 4,000,000 but sometimes getting down to 2,000,000. Such a low count generally indicates some complication. The red cells are usually smaller than normal, very pale in the center and frequently show poikilocytosis. Nucleated red cells rarely appear, when they do the normoblasts is the common type, although megaloblasts have been found. The specific gravity is reduced in proportion to the decrease of hemoglobin, it may reach 1028.

Changes in the leukocytes in size and number are unusual.

Pernicious anemia is a disease of the blood and blood-forming organs, characterized by excessive destruction associated with defective production of red cells. The amount of hemoglobin is diminished greatly at the same time but the amount in each red cell is usually greater than normal, thus giving a high color index, more frequently above one than below.

The cause of this condition is unknown although in some instances there has been an infection by intestinal parasites, particularly the Dibothriocephalus latus and the Uncinaria duodenalis. A similar blood picture has also been found as a result of numerous hemorrhages, of gastric carcinoma, and of atrophy of the gastric mucosa. The destruction of the blood may take place chiefly in the portal circulation and especially in the spleen as the result of toxic substances absorbed from the intestine. It has also been noted that certain anërobic bacteria found in the large intestine produce a substance that has marked hemolytic properties. This penetrates the wall of the intestine and enters the portal circulation.

The blood shows a marked diminution of erythrocytes

often as low as 1,000,000 or even lower, 138,000. The hemoglobin is considerably reduced, 25 to 35 per cent. being common, but the relative amount in each cell is high.

There are also decided variations in the size of the red cells, megalocytes being very numerous; microcytes are also common. Nucleated red cells also occur in large numbers, the megaloblasts usually outnumbering the normoblasts. This pre-

FIG. 127.—PERNICIOUS ANEMIA (Cabot).
L, *L*, Lymphocytes; *m*, *m*, *m*, *m*, megaloblasts; cover-slips stained with Ehrlich's triacid, and drawn with camera lucida.

ponderance of the megaloblasts is practically pathognomonic of this type of anemia. The nuclei are frequently degenerated and generally show polychromatophilic degeneration. Poikilocytes are very common, numerous, and show a great variety of shapes.

Coagulation is slow, specific gravity is low, 1.028, and there is little tendency to form rouleaux.

The leukocytes are generally somewhat decreased in number, averaging about 4000. This condition is practically never present in the secondary anemias. An increase in number indicates, as a rule, some complication. The decrease is mainly in the polymorphonuclear type and consequently there is a relative increase in the number of lymphocytes. A few myelocytes may be found.

On account of the extensive destruction of the red cells with the consequent liberation and breaking down of the hemoglobin there is an extensive deposit of iron in the liver, spleen, marrow and other organs. On account of the lessened oxygen the chief lesion of the tissues is an extreme fatty degeneration of the viscera, particularly the liver, kidneys and heart muscle. The marrow of the long bones is no longer yellow, but red, and soft, and frequently shows areas of hemorrhage. Under the microscope it will be noted that the normal nucleated red cells are in part replaced by an excessive number of megaloblasts, large nucleated red cells. There is also a greatly decreased amount of fat in the marrow. In the spinal cord degeneration of the posterior columns has been described and is thought to be due to minute hemorrhages.

Splenic anemia is a form of chronic anemia characterized by an idiopathic enlargement of the spleen without any involvement of the lymph nodes. In *Banti's* disease there is the primary increase in size of the spleen with a secondary interlobular (portal) cirrhosis of the liver.

The blood shows a relatively high red cell count, a marked reduction in the percentage of hemoglobin, and a low color index. The white cells are usually decreased, but there is a relative lymphocytosis.

In the *Gaucher* type of splenomegaly there is a wide-spread proliferation of the endothelial lining of the splenic sinuses. The blood may contain large numbers of nucleated reds, with a high leukocytosis, and a small percentage of myelocytes. This disease usually occurs in children.

Pseudoleukemia infantum is a rare form of anemia seen in children and is characterized by an enlargement of the spleen,

liver, and lymph nodes. The red cells are greatly reduced, to about 1,000,000, nucleated erythrocytes are common, hemoglobin is diminished, and the leukocytes increased to 20,000 to 50,000. This latter vary greatly in shape and frequently are much larger than normal.

Secondary anemia is one in which there can be found an underlying cause to explain the changes present in the blood. The hemoglobin is regularly diminished to a greater extent than the red cells; it may fall as low as 15 to 20 per cent. The red cells seldom fall below one million. In severe cases normoblasts may be numerous. The size of the red cells is slightly below the normal, and there is usually some poikilocytosis. As a rule there is not much change in the leukocytes unless suppurative processes are present. The specific gravity is reduced in direct proportion to the loss of hemoglobin. The rapidity of coagulation is commonly increased.

The more common causes are acute and chronic hemorrhage, inanition, intestinal parasites, fever and certain poisons such as alcohol, lead, acetanilid and others that cause hemolysis with hemoglobinemia.

Leukemia is a disease of the blood-producing structures, characterized by a permanent increase in the leukocytes other than the polymorphonuclear variety, and by lesions of the bone marrow and hyperplasia of the lymphoid tissues.

The cause is unknown.

According to the type of leukocyte predominating in the blood, leukemia may be *myelogenous*, *lymphatic or mixed*, when the two varieties are present. The disease may be also either acute or chronic.

In the *spleno-medullary* (*myelogenous*) type the myelocytes are present in great numbers, constituting from 20 to 60 per cent. of all leukocytes. The total number is about 300,000 per cubic millimeter as an average, but counts as high as 750,000 have been reported. The number, however, may be as low as 100,000 or even in some the count may approximate the normal. The differential count of the white cells in combination with the usual increase in number is the characteristic feature. The main form is the large mono-

nuclear myelocyte containing neutrophilic granules. They may constitute some 35 per cent. of all the leukocytes. The nucleus is situated, as a rule, in the center and is well staining, it may be excentric, however, or poorly staining. The large cell with the pale nucleus is seldom found in any other condition than in this form of leukemia. The neutrophilic granules may be lacking entirely and the nuclei show hydropic de-

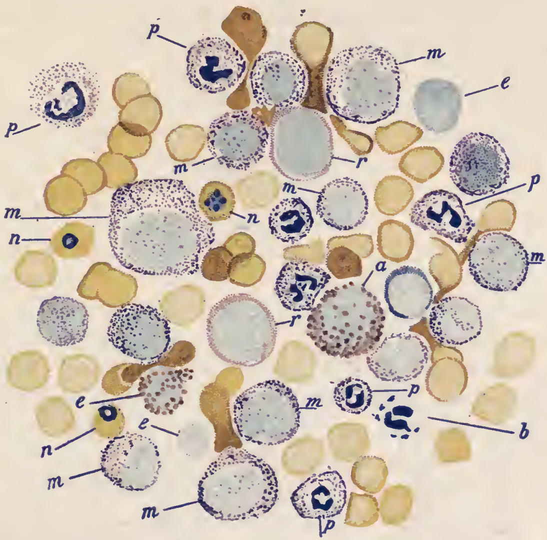

FIG. 128.—MYELOGENOUS LEUKEMIA (Cabot).

a, Eosinophilic myelocytes; *b*, "mast-cell;" *e*, *e*, *e*, ordinary eosinophile; *m*, *m*, myelocytes; *n*, *n*, normoblasts; *p*, *p*, polynuclear neutrophiles; *r*, *r*, Reizungsformen (Türck) (cover-glass film stained with Ehrlich's "triacid" and drawn with camera lucida).

generation. Occasionally small myelocytes with deeply staining nuclei may be present.

Eosinophilic myelocytes may be found in large numbers, varying from 3000 to 100,000 per cubic millimeter. Such an increase is pathognomonic of splenomyelogenous leukemia. The ordinary type of eosinophiles is also increased.

Basophiles or mast-cells are increased, sometimes very

markedly, this condition being quite characteristic of the leukemia.

Polymorphonuclear neutrophilic leukocytes are relatively diminished as the myelocytes increase, and form about 46 per cent. of the total. They are absolutely increased to 60,000 or 70,000. Degenerative changes are very common, the cells becoming more cohesive, the nuclei pale and showing karyolysis or rhexis, and frequently mitotic figures.

Lymphocytes are not very numerous as a rule; they constitute about 10 per cent. although the number may vary considerably.

The blood itself may be pale and the specific gravity lowered. Coagulation takes place slowly. The erythrocytes are decreased to about 3,000,000, the hemoglobin is diminished also, 40 per cent., color index about 0.6. Many of them are nucleated and show changes in size and shape. The normoblasts are very common, and megaloblasts are frequently seen.

The organs involved are the spleen and bone-marrow. The latter shows a marked hyperplasia, loses its yellow color and becomes dark red. Numerous nucleated erythrocytes and eosinophiles are present. The spleen is much enlarged as a result of a general hyperplasia of both the connective and lymphoid tissues. Grayish, circumscribed areas, due to the infiltration of leukocytes, may be seen. The liver is usually somewhat enlarged, and the lymph nodes may show some hyperplastic changes. Hemorrhages into the serous and mucous membranes and the retina are quite frequent. Fatty degeneration of the viscera generally occurs to some extent.

In *lymphatic* leukemia the lymphocytes constitute from 80 to 90 per cent. of all leukocytes which number about 145,000 per cubic millimeter. The lymphocytes are usually of the small mononuclear type with a narrow rim of protoplasm around a fairly deeply staining nucleus. Sometimes the large type predominates, these latter being found more generally in acute cases and in children. In this form of leukemia, polymorphonuclear leukocytes, myelocytes, eosinophiles and mast-cells are few.

The anemia in this form is more marked than in the other, the red count at times being down to 1,500,000 with a hemoglobin per cent. of about 37. Nucleated red cells are very scarce except in the very severe cases when they may become numerous.

The lymph nodes show marked hyperplasia and enlargement, and the spleen, although enlarged, seldom reaches the size that it does in the spleno-myelogenous type.

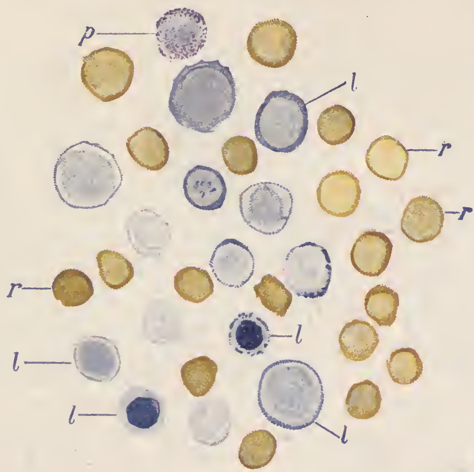

FIG. 129.—LYMPHATIC LEUKEMIA (Cabot).
l, *l*, *l*, *l*, *l*, Lymphocytes; *p*, polynuclear neutrophile; *r*, *r*, *r*, red cells.

Pseudoleukemia.—Under this term are included a great variety of diseases which may show gross changes similar to those of leukemia, yet with none of the characteristic blood changes. *Hodgkin's disease*, although an inexact term, has come to signify a condition in which there is a progressive increase in the size of the lymph nodes, particularly the cervical, axillary and mediastinal, with the blood changes present in leukemia. The blood shows a slight diminution in the number of red cells, 3,000,000 to 4,000,000, and a decreased

hemoglobin percentage. The leukocytes are slightly increased, averaging about 12,000.

Microscopically the bone-marrow shows a moderate hyperplasia. The lymph nodes undergo some hyperplasia and show areas containing numbers of large cells with a faintly staining cell body and a single large nucleus. Later in the disease will be found necrotic areas surrounded by cells of the epithelioid type and more or less numerous large cells with polymorphic nuclei or with two or more small oval nuclei lying in the center of the cell body. Accompanying this is

FIG. 130.—HODGKIN'S DISEASE (Stengel).

Showing marked enlargement of the glands of the right axilla, with consequent dropsy of the arm; less marked involvement of the submaxillary and cervical lymph-glands.

an increase of the connective tissue. Eosinophile cells are present in the lymph nodes usually in great numbers.

The cause of this disease is not known. The condition seems to be related, more or less closely, to leukemia and lymphosarcoma. Mallory discards the above terms and refers to pseudo-leukemia and Hodgkin's disease as *lymphoblastoma*, tumors of mesoblastic origin in which the cells tend to differentiate into lymphocytes, or into cells of the lymphocyte type.

CHAPTER XIX

DISEASES OF THE CIRCULATORY SYSTEM

DISEASES OF THE HEART

Congenital malformations may be the result of disturbances of development or of disease during fetal life.

There may be complete absence, as in acardiac monsters. Imperfect septa between the cavities is the most common defect. There may be no septum and a simple heart of two cavities, like that of a fish, is formed. If the ventricular septum is absent there are two auricles and one ventricle, the reptilian type. The auricular septum is often incompletely closed, giving rise to a open ~~patulous~~ foramen ovale. The heart may be completely reversed, lying on the right side of the body with the aorta coming from the right ventricle and the other vessels correspondingly shifted. Is known as dextrocardia.

The arterial openings may be much smaller than normal, particularly the pulmonary. When the latter occurs there is marked cyanosis. If the stenosis is of a high grade the pulmonary circulation may be maintained by a persistent ductus arteriosus. Gives rise to hypertrophy of the right ventricle.

The valves may vary in number and also in length.

Diseases of the Pericardium.—May have *hydropericardium*, a collection of non-inflammatory transudate within the sac. This is usually a part of a general dropsy due to disease of the heart, kidney or liver. *Hemopericardium*, when containing blood which gains entrance from rupture of the heart, of aneurysms of the great vessels or wounds. If in large amount it causes death by mechanically interfering with the contraction of the heart.

Pericarditis is seldom primary, but is usually secondary to infectious diseases, such as acute rheumatism, scarlet fever, pneumonia, endocarditis and pyemia. It may result from the extension of inflammation from neighboring tissues.

FIG. 131.—ACUTE PERICARDITIS (Bramwell).

The inflammation may vary greatly, and according to the exudate various forms of pericarditis are described such as fibrinous, serofibrinous, and purulent. There is at first a dulness of the serous membrane as a result of changes in the

endothelium and the formation of a delicate layer of fibrin, and later a serofibrinous exudate. This may be slight or there may be 1000 to 2000 c.c. of fluid. The pericardium may become thickened, roughened, and covered by a coating of fibrin that may be quite marked. At the apex the fibrin is collected into strands, giving a villous appearance to the heart, the *cor villosum*. At the base of the heart, where the movements are more restricted, there is a "bread and butter" appearance.

As the serum is absorbed the fibrin may be replaced by connective-tissue adhesions until the pericardial sac is either partially or completely obliterated, *adhesive pericarditis*. As a result of this, marked hypertrophy may ensue and also some degeneration of the myocardium. Occasionally there is a deposit of lime salts in the organized tissue.

In the early stage there is microscopically a degeneration of the endothelium, which is covered by a layer of fibrin, and a round-cell infiltration of the subendothelial tissue.

Purulent pericarditis generally results from the extension of suppuration of some neighboring organ. The most common organisms found are the streptococci, diplococci pneumoniæ, staphylococci and the tubercle bacilli. It may start as a simple inflammation and later on give rise to a purulent exudate. The pericardial sac contains more or less purulent or seropurulent fluid. The myocardium is usually involved superficially; it becomes edematous, infiltrated with pus, and may undergo fatty degeneration; at times inflammation, myocarditis, may occur.

Tuberculous pericarditis is commonly a part of a general miliary infection, or it may result from an extension from a neighboring lesion of the pleura. The exudate is frequently blood-stained. Both the visceral and parietal layers of the pericardium may show considerable thickening. The lesions found are similar to those occurring in tuberculosis in other parts.

Milk spots are irregular whitish areas found on the external surface of the heart. They probably result from constant pressure and are more accurately known as friction scleroses.

Some may be the results of a previous inflammation. There is a thickening of connective tissue below the endothelium.

Tumors.—Sarcoma and carcinoma occur as secondary growths either from infiltration or as metastatic tumors.

Myocarditis or inflammation of the heart muscle is usually secondary to infectious conditions elsewhere, particularly in pericarditis. May be acute or chronic, diffuse or circumscribed.

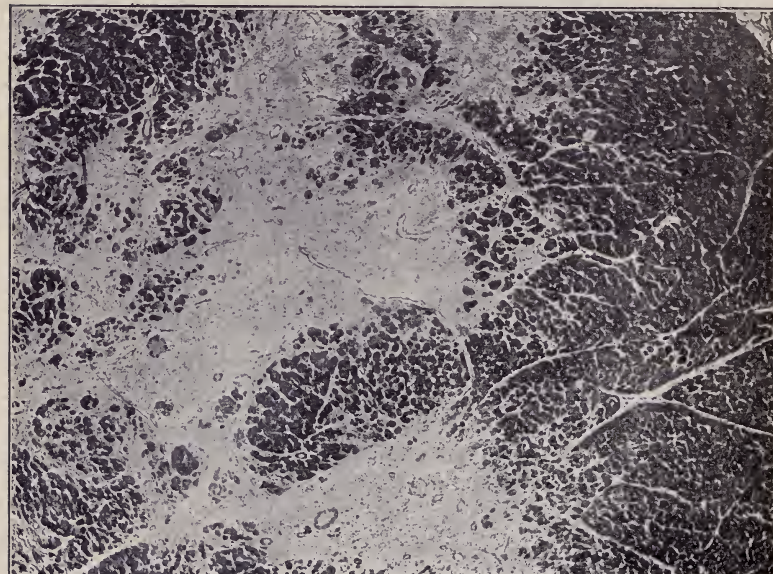

Fig. 132.—Chronic Interstitial Myocarditis.
(Fibrous replacement hyperplasia.) [Delafield and Prudden.]

In the *acute circumscribed* form numerous small metastatic abscesses are present. Beginning as minute infectious emboli in small vessels, generally in cases of malignant endocarditis, degeneration and necrosis may ensue, so that an abscess cavity the size of a cherry may develop. The contents are composed of pus, broken-down muscle and bacteria. This may perforate into the cavities of the heart, into the pericardium, or may form a cardiac aneurysm. The abscess may lose its

liquid contents, become encapsulated or infiltrated with lime salts.

In the *acute diffuse* variety, as seen in diphtheria and scarlet fever, there is a diffuse round-cell infiltration between the muscle fibers with proliferation of the connective-tissue cells as well. The muscle fibers become granular, opaque, and the striations indistinct: They may undergo Zenker's hyaline degeneration. If the patient recovers scar tissue may form. This condition occurs in scarlet fever, diphtheria, typhoid, gonorrhea, etc.

The heart is soft and friable, and usually lighter in color than is normal, and the fibers are easily separated. Dilatation of the left ventricle is often present.

In *chronic fibrous myocarditis* the lesions may be diffuse or localized. It may be the result of a former acute diffuse myocarditis or it may be secondary to diseases of the coronary arteries or to disturbances of their circulation. This leads to degeneration or necrosis of the muscle and a new formation of fibrous tissue, a replacement hyperplasia, probably not inflammatory. In the muscle are seen spots or streaks of sclerotic tissue. Microscopically greater or less amounts of connective tissue are found separating the fibers which frequently undergo a fatty degeneration as a result of pressure and thus give rise to irregular yellowish areas.

Some of the sclerotic portions found along branches of the coronary artery probably represent healed infarcts.

Fatty metamorphosis is often found in toxic and infectious diseases. Is usually irregular in its distribution, forming areas of yellowish tissue, easily distinguished beneath the endocardium. In the fibers are found fat granules; the striations disappear and the nuclei may show degenerative processes. The muscle becomes soft and flabby.

Brown atrophy is a condition in which the heart is reduced in size and is brownish-red in color. Is found in old age and in chronic cachexias. Within the muscle fiber at the ends of the nuclei are found numerous minute brownish granules (Fig. 11).

Necrosis, myomalacia cordis, of the heart muscle is usually

due to obstruction of the coronary artery by arteriosclerosis, thrombosis, or embolism with the formation of an infarct. The wall at the apex of the left ventricle is the common site. This area breaks down, and empties into the ventricle or into the pericardial sac. May rupture or may dilate and form a cardiac aneurysm.

By **endocarditis** is indicated an inflammatory condition of the serous membrane lining the heart. Is most common upon the valves (valvular), although the endocardium of the cavities (mural) may be involved. It may be divided into the *acute* and the *chronic*, the acute being subdivided into the *verrucous* and the *ulcerative*.

Acute endocarditis is a secondary condition occurring in the course of an infectious disease as a result of the action of bacteria. It is characterized by the formation of cauliflower growths upon the valves or by ulceration of the leaflets.

It is found particularly in acute articular rheumatism, chorea, in pneumonia, scarlet fever, puerperal sepsis, and gonorrhea. The organisms most commonly found have been the staphylococcus, streptococcus, and diplococcus pneumoniæ, also the gonococcus. In many cases the bacteria probably gain entrance through the tonsils.

The most common seats are the mitral valve, then the aortic and pulmonary valves. In fetal endocarditis the right side of the heart is more frequently involved. Instead of the edge the lesion first occurs on the line of closure. The endocardium becomes opaque and small, irregular nodules appear (*verrucous endocarditis*). These elevations consist of layers of fibrin, beneath which is the endocardium, showing desquamation of the endothelium with also round-cell infiltration and proliferation of the fixed connective-tissue cells. In the masses of fibrin will be found blood plates, leukocytes, and frequently bacteria.

The process may terminate by a degeneration of the vegetations with the formation of scar tissue and subsequent thickening and contraction. There may also be marked calcareous infiltration.

If the condition continues there may be destruction of the

valve, *ulcerative endocarditis*. In this there is a superficial necrosis of the valve with a deposit of fibrin upon the ulcerated surface. As the lesion progresses the leaflet may become weakened and distended by the blood-pressure, forming an aneurysm of the valve. Perforation may occur and portions of the leaflet, or of the fibrin mass, may be set free in the blood

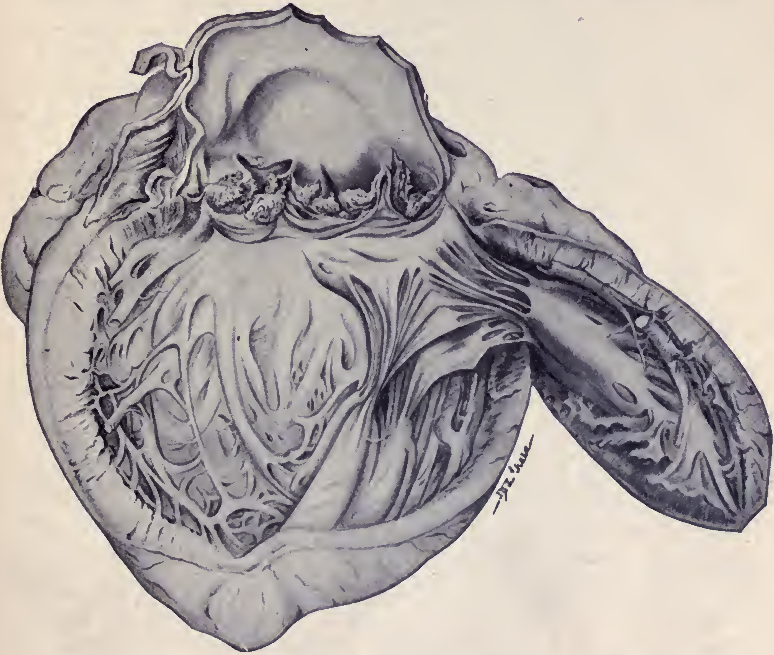

Fig. 133.—Chronic Verrucous Endocarditis of the Aortic Valves, showing the Warty Projections from Their Edges. The Valves are at the Same Time Thickened and Stiffened by Sclerotic Changes (McFarland).

as emboli. These generally contain bacteria, and, lodging in the brain, kidney, and spleen, will give rise to metastatic abscesses.

Either of these two varieties may terminate in the chronic form.

In *chronic* or *sclerotic* endocarditis there is an overgrowth of fibrous tissue, usually with calcification, causing a distortion of the valves. The leaflets become thickened, less elastic, rigid and hard, and frequently shortened. As a result the lumen of the orifice may be decreased and give rise to obstruction to the flow of blood (*stenosis*). On account of the lack of elasticity the valves are no longer able to completely close the orifice, so there is a backflow of blood (*regurgitation*).

There is also frequently present a shortening and thickening of the chordæ tendineæ, which on account of preventing the valves from closing gives rise to regurgitation.

This form of endocarditis may be a sequel to the acute varieties, or it may gradually develop independently of such conditions, as in gout, chronic rheumatism, alcoholism, and syphilis.

There may also be bits of tissue or fibrin broken off, with resulting embolism.

As a result of the disturbances of the circulation which call for increased effort, there is hypertrophy of the heart, with subsequent dilatation.

CARDIAC HYPERTROPHY

In this condition there is an increase in both the number and size of the muscle fibers. It may be the result of either *outside* interference to the heart's action, as in adhesive pericarditis, particularly if pericardium is also adherent to surrounding tissues; or *inside* resistance, as occasioned by valvular lesions. It also occurs when there is increased resistance to the flow of blood, as is found in arteriosclerosis.

Hypertrophy will, however, occur only when the heart is primarily able to overcome the obstacle. If unable to do so, there will be relaxation, dilatation. As a rule, one chamber of the heart is chiefly involved, but it is unusual not to find other chambers more or less affected.

When the heart enlarges sufficiently to overcome its obstructions and the circulation is carried on without any apparent trouble, the condition is known as *compensatory hypertrophy*. This may continue for a long time, but there finally

comes a moment when the heart is no longer able to do its work. The symptoms then of failure of compensation make their appearance.

According to the location of the obstacle different cavities of the heart are involved. In the most common valvular

FIG. 134.—HYPERTROPHY AND DILATATION OF THE HEART (Bollinger).

lesion, mitral regurgitation, there is a hypertrophy of the left ventricle. In lesions of the aortic valve the greatest enlargement may occur, giving rise to the "cor bovinum." Enlargement of the left ventricle may follow stenosis of the aorta, from an increased resistance to the flow of blood through

the peripheral arteries as in various forms of arteriosclerosis or obliterating endarteritis, and from certain forms of nephritis.

Enlargement of the right ventricle arises from interference with the circulation within the lung, as in emphysema, chronic bronchitis, and asthma.

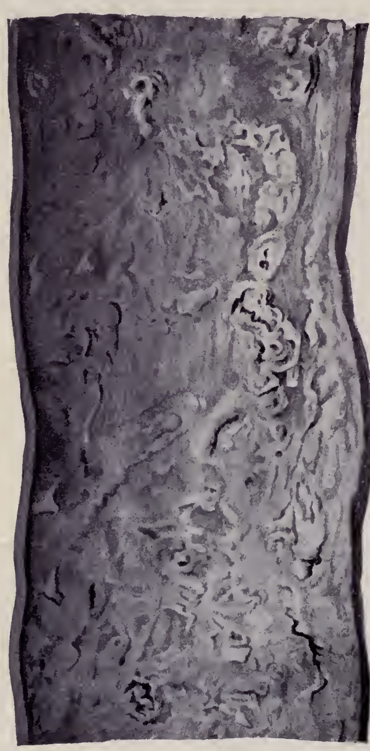

FIG 135.—ATHEROMA OF THE AORTA (Bollinger).

The hypertrophy resulting from valvular lesions is due to the cavity containing a greater amount of blood than is normal, whether stenosis or insufficiency or both be present. If there is stenosis, the entire charge of blood is not pushed forward before the heart enters into diastole and receives another supply from the auricle. If there is regurgitation the ventricle during its diastole receives blood both from the auricular and from the distal sides. In either case the heart must increase its muscular power before the circulation can be properly carried on.

The hypertrophied heart may weigh as much as 1000 or 1500 grm. in extreme conditions, more commonly from 700 to 800 grm.

Three forms of cardiac hypertrophy may be described:

I. *Simple hypertrophy*, in which there is an increase in the thickness of the muscular wall without any diminution in the capacity of the cavity.

II. *Excentric*, in which there is increase in the size of the cavity and in the thickness of the walls.

III. *Concentric*, in which there is thickening of the wall with diminution in the cavity. This is probably a pure post-mortem finding, being an arrest in systole of a hypertrophied heart.

CARDIAC DILATATION

This may be either *acute* or *chronic*, *active* or *passive*.

The *acute* form occurs as a result of severe muscular exertion or from a sudden interference with the passage of the blood through the pulmonary circulation.

The *chronic* is generally associated with hypertrophy and is referred to also as *active* in that the dilatation is associated with a thickening of the muscle wall.

In *passive* dilatation the increase in size of the cavity is accompanied by a thinning of the wall. This may be due to valvular interference, to changes in the muscle tissues of the heart and to all conditions that interfere suddenly with the emptying of the heart.

Dilatation is due either to a *weakening of the cardiac walls*, following interferences with nutrition, or to an *increase in the cardiac blood-pressure.*

The failure of nutrition generally is due to interference with the coronary arteries. In this the heart walls become soft and flabby, and in consequence dilate.

DISEASES OF THE ARTERIES

Endarteritis, or inflammation of the artery, usually results from the presence of foreign bodies, either infectious or sterile, within the vessel. It may be caused by organisms gaining entrance into the vasa vasorum. The intima is first involved; it becomes roughened, the endothelial cells become loosened, and there is usually an infiltration of round cells. The vasa vasorum are involved and the inflammatory process may extend to the media or the adventitia, and as a result a thrombus generally forms within the lumen. This may undergo organization with connective-tissue formation within the lumen of the vessel—*thromboarteritis proliferans.*

Periarteritis is an inflammatory condition around an artery, usually arising from injuries from without, or sometimes by extension from within. There is an infiltration of the adventitia, which becomes swollen and edematous. The media and intima become involved, there is desquamation of the endothelium with the formation of thrombi, usually infectious.

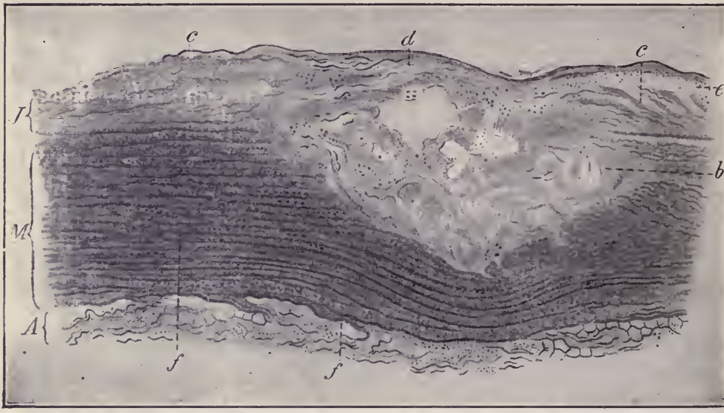

FIG. 136.—AN ATHEROMATOUS PATCH IN THE ABDOMINAL AORTA WHICH HAS NOT YET BROKEN THROUGH (Dmitrijeff).

J, Intima; *M*, media; *A*, adventitia; *b*, atheromatous necrotic focus in the intima and media; *c*, elastic fibers of the intima; *d*, elastic fibers which have persisted between the necrotic focus and the endothelial layer; *e*, thickened endothelium; *f*, infiltration of the media with small cells.

Arteriosclerosis, arterio-capillary fibrosis, or chronic arteritis, is a condition characterized by an increase in connective-tissue formation accompanied by degenerative changes. These may be circumscribed or diffuse. The fibrous formation occurs chiefly in the outer coats and is referred to as *sclerosis*, the degenerative processes involve the sub-intimal tissue and are spoken of as *atheroma*.

The large vessels such as the aorta, particularly the arch, are most commonly affected, but the arteries at the base of the brain and the splenic artery are frequently involved. Such an

involved vessel, as the aorta, is usually dilated and the intima greatly roughened. The surface appears mottled on account of the varying changes from the normal yellowish streaks of atheroma, pale areas of sclerosis and calcification will alternate with reddish collections of fibrin.

In the circumscribed form, *arteriosclerosis nodosa*, numerous small oval or round yellowish-white areas are visible. These are but slightly elevated and vary in their consistency according to the structure. If there is much connective tissue, they may be very firm, almost cartilaginous; if degenerative changes have occurred, they will be soft.

As a result of the presence of these areas the elasticity of the vessel is interfered with, nutrition suffers, and connective tissue forms. Beneath the intima this new-formed fibrous tissue, which is usually dense, tends to undergo fatty degeneration, to become necrotic and to degenerate. In this way large or smaller cavities, filled with a softened semi-fluid substance consisting of disintegrated tissue, fat, and cholesterin crystals, develop. They are called *atheromatous cysts* and are covered by an imperfect layer of endothelium. This covering may break off, allow the contents to escape, leaving a cavity known as an *atheromatous ulcer*. The material found within these so-called cysts is composed of tissue that has undergone a fatty degeneration. Microscopically yellowish granules and droplets of fat as well as crystals of fatty acids are present. Instead of escaping, the cystic contents may become markedly infiltrated with lime, thus forming *atheromatous plates*.

Whenever an atheromatous ulcer has formed, the wall of the vessel at that point may be thinner and less elastic than normal. Eventually there may be a proliferation of the connective-tissue coat to give support to the weakened area. As the elasticity of the vessels is decreased there is consequent increase in blood-pressure with hypertrophy of the left ventricle. With the increased pressure there occur dilatations of the vessel at its weakened points, with the formation of aneurysms.

In the smaller vessels, particularly of the brain, rupture or apoplexy quite frequently occurs.

In *diffuse arteritis* or *arterio-capillary fibrosis* the smaller arteries and capillaries are the seat of fibrous tissue formation. Resulting from this, there may be more or less diminution of the lumen of the vessel, *endarteritis deformans.*

If the lumen is completely occluded, is known as *endarteritis obliterans.* In both cases there will be interference with the supply of nutrition and degenerative changes, chiefly hyaline, of varying degree consequent.

These lesions are very common in both syphilis and tuberculosis. In the first there is a cellular proliferation beginning in the adventitia but ultimately involving the intima.

Aneurysm.—An *aneurysm* is a circumscribed dilatation of an artery. It may be (1) *true* or (2) *false. True,* an aneurysm

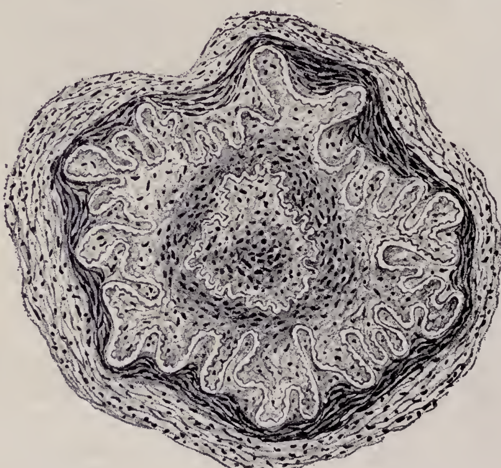

Fig. 137.—Endarteritis Productiva (Dürck).

in which the sac is formed by the arterial walls, one of which at least is unbroken. *False,* one in which all the coats are ruptured, the blood being retained by the surrounding tissues.

Aneurysms may be single or multiple, and may vary greatly in size. They result either from injury or disease of the vessel or from increased arterial blood-pressure.

They are classified according to their form. They may be:

1. *Saccular*, in which case there is a hemispherical dilatation extending from one side of the artery. As a result of the dilatation the middle coat soon atrophies, the inner coat is generally destroyed by an endarteritis so that the outer coat alone usually forms the wall of the aneurysm.

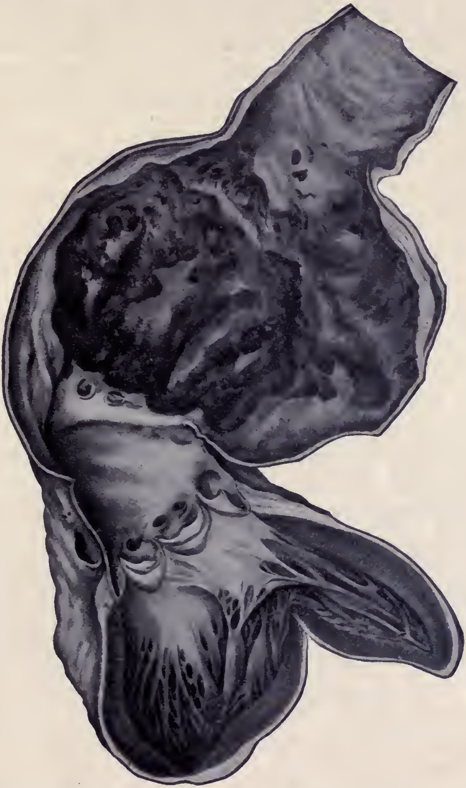

FIG. 138.—ANEURYSM OF THE ARCH OF THE AORTA (Bollinger).

2. *Fusiform*, a cylindric dilatation extending for some distance along the artery. Are most common in the aorta.

3. *Dissecting*. In this variety the blood passes through an opening in the diseased intima and makes its way between it

and the media, or between the media and adventitia. Occasionally the blood may re-enter the lumen through a lesion further along in the course of the vessel. Is most common in the large arteries.

4. *False*. Following an injury to an artery, a wall of fibrous tissue may form around the escaped blood, while the wound in the vessel remains open, so that there is an aneurysmal sac through which the blood is constantly flowing.

In the brain there is quite frequently found a condition known as multiple miliary aneurysms. In the course of the small vessels, particularly branches of the lenticulo-striate, numerous very small dilatations may be found. They are probably the result of degenerative changes in the media.

After an aneurysm has once been formed it may be rendered harmless by means of the deposition of layers of fibrin within the cavity. This may go on till there is complete obliteration; this, however, does not frequently occur as the deposit of fibrin cannot keep step with the dilatation of the vessel. Although an aneurysm is a soft structure there may be extreme destruction of surrounding tissues, particularly of bone. The pressure exerted by the aneurysm shuts off the periosteal blood-supply and more or less erosion of the bone follows.

Ultimately rupture of the sac generally occurs. The walls have become so thinned and weakened that they are no longer able to resist the pressure. Rupture commonly takes place when there has been some unusual muscular exertion. It may occur, though, when the individual is quiescent.

DISEASES OF THE VEINS

Thrombosis has already been discussed under that general heading.

Phlebitis, inflammation of the veins, may follow inflammatory conditions around the vessel, from traumatism, or it may arise from conditions within, by infection from microorganisms circulating in the blood. It may be an *acute purulent* form in which there is first an infiltration of round cells, then rapidly of pus cells. This condition follows along the

vessel, forming abscesses and thrombi. The formation of the latter depends upon the loss of integrity of the intima. The thrombi act as plugs so as to prevent as well as possible the entrance of the invading organisms into the blood, but they may break down and send forth innumerable particles of infecting material.

Chronic phlebitis, or *phlebosclerosis*, is a condition similar to arteriosclerosis, but is much less common. In it the sclerotic processes predominate, the atheromatous being less marked.

Varicose veins are ones in which dilatation has occurred. This may take place in the neighborhood of a valve, and by rendering it incompetent the blood-pressure is increased. In this way the greater part of a vein may be distended. If the vessel has become longer than normal it will naturally be more tortuous (cirsoid). In this form the various loops may come in contact, and at that point undergoing atrophy of their walls communications will be established; these are known as *varices*, or *varix*. Such portions resemble cavernous or erectile tissue.

In the dilated portions thrombi may form or a periphlebitis with the formation of dense connective tissue take place. *Phleboliths*, thrombi that have undergone calcification, are quite common.

Interference with the venous return seldom leads to as severe results as corresponding lesions in the arteries. This being due to the readiness with which collateral circulation can be established. Varicose veins are most common in the lower extremities. There is generally edema present, and if a skin surface is involved extensive ulcerations may form. These ulcers heal with difficulty on account of the poor nutrition. Another result of venous congestion is the formation of dense connective tissue.

The varicose condition is the result of disease of the vessel wall or of increased venous pressure, brought about by interference with the return flow. This is well seen in the long veins of the lower extremity.

Special names have been given to varicose conditions of

certain veins. Dilatation of the spermatic veins is known as *varicocele;* of the hemorrhoidals, as *hemorrhoids.*

LYMPHATICS

Inflammation of the lymph-vessels, *lymphangitis,* is nearly always secondary to bacterial infection. It frequently follows superficial injuries, particularly those received in the making of autopsies. It appears clinically as reddish streaks extending from the point of infection, the result of a perilymphangitis. The inflammation may go so far as to involve distant lymph-nodes, which become swollen, tender, and sometimes suppurate.

The lymph-vessels may become dilated, *lymphangiectasis.* Is usually due to obstruction by parasites. Is found in elephantiasis.

If there is any defect in the wall of the vessel the lymph may escape into an adjoining cavity or upon the surface of the body. When it enters the abdominal cavity chylous ascites ensues.

Tuberculosis of the lymphatics, particularly when there is tuberculosis of the serous membranes, is common. The vessels appear as grayish lines.

Syphilis commonly involves the lymph-nodes in all its stages.

CHAPTER XX

DISEASES OF THE RESPIRATORY SYSTEM

DISEASES OF THE NOSE

Malformations of varying degrees of severity, from complete absence to slight cleft lip, may exist. There may be no external abnormality, but the floor of the nasal cavity may be lacking, the septum deviated, or there may be complete obstruction to one or both nostrils by bony growths.

Rhinitis or **coryza** is an inflammatory condition of the mucous membrane of the nose. It may be acute or chronic and may be caused by direct or indirect influences.

The *acute* form is generally attributed to cold, but may be brought about by exposure to the inhalation of various irritating bodies, as pollen of flowers or the fumes of various chemicals, by the action of micro-organisms, or by vasomotor disturbances.

There is first a condition of hyperemia and dryness of the nasal mucosa, which is soon followed by a discharge that is serous, seromucous, or mucopurulent in character. This may cause excoriation of the tissues that it comes in contact with. In the discharge are found epithelial cells and leukocytes as well as bacteria.

Chronic rhinitis usually follows repeated attacks of the acute form, but may be due to some abnormality of the nose itself. It may be of two forms, the hypertrophic and the atrophic.

In the *hypertrophic* variety there is congestion of the veins with thickening and swelling of the mucosa. The mucous glands increase in size, there is a thick, viscid secretion, and the nasal passages are much obstructed, particularly by enlargement of the lower turbinated bones. There is also a hyperplasia of the connective tissue.

The *atrophic* form may follow in the course of the hypertrophic. The hyperplastic fibrous tissue shrinks, the epithe-

lium of the mucosa and the glands are destroyed, and there is a secretion of a yellowish purulent matter. This latter has an extremely disagreeable odor; the condition is termed ozena. The bony septum may even be destroyed. In the discharge saprophytic organisms as well as others may be found.

Diphtheria may involve the nasal mucosa primarily, but usually is secondary to the pharyngeal form. In it there is a pseudo-membrane formed and the organism of diphtheria can be found.

Syphilis generally occurs in the form of a coryza that does not differ from that arising from other causes. In the later stages ulceration with necrosis of the bones may occur. Gumma situated within the periosteum or perichondrium may form. This is often followed by destruction with the sinking in of the bridge of the nose.

Tuberculosis may give rise to ulceration with subsequent necrosis. In the discharges the tubercle bacilli can be demonstrated.

Leprosy is said to be first demonstrable in discharges coming from ulcerations of the nose.

Glanders may be conveyed from a diseased horse to the nasal mucosa of man and give rise to nodules or farcy buds.

Tumors.—The most common form is that known as a *polyp*. Polyps are composed of fibrous tissue, that is generally myxomatous, and a covering of mucous membrane. These growths may be mucous, adenomatous, cystic, or telangiectatic.

Various forms of connective-tissue tumors, as the fibroma, chondroma, osteoma, and sarcoma, occur. The *fibroma* may give rise to severe hemorrhage if it is highly vascular. The *sarcoma* is the most common malignant tumor. It may arise from the septum, but more frequently it extends from the antrum.

Carcinoma is not so common, but epitheliomata may develop at the junction of the skin and mucous membrane.

Chondritis and *perichondritis* are inflammations of the cartilages of the larynx secondary to ulcerations of adjoining tissues. The cartilages, being very poorly supplied with blood, have their nutrition interfered with by the inflamma-

tory conditions and degenerative changes ensue. In old age the cartilages may undergo calcification.

DISEASES OF THE LARYNX

Malformations of the larynx are neither numerous nor specially important. The parts may be unsymmetric or there may be a fistula resulting from the imperfect closing of a branchial cleft.

Acute laryngitis or inflammation of the larynx results from exposure to cold, from inhalation of irritating vapors and substances, or is due to infections secondary to disease of the mouth, pharynx, or lung. It begins with a congestion and swelling of the mucosa. This is followed by increased secretion with disturbances of the voice due to involvement of the vocal cords. There is a round-cell infiltration of the tissue with sometimes ulceration, in the healing of which scar tissue forms.

Chronic laryngitis often follows acute attacks or it may develop independently. In it there is dilatation of the vessels and hypertrophy of all the portions of the mucosa. There is a slight thick secretion and the membrane looks distinctly granular on account of the swollen glands, *granular laryngitis*. Is generally found in singers and lecturers.

Edema may occur slowly, as in passive congestion and in chronic inflammations, or it may take place very rapidly (*acute edema of the glottis*) as a result of some sudden and severe inflammatory process, as from the inhalation of steam, gases, or the action of irritating substances. In it there is a serous infiltration of the arytenoid cartilages and the aryteno-epiglottic folds. These swollen tissues meet in the middle and more or less completely obstruct the passage of air into the lungs, sometimes causing death.

In **diphtheria** of the larynx, which may be primary or secondary to that of the pharynx, there is an acute inflammatory process with marked exudation. This contains much fibrin and, undergoing coagulation, forms a pseudo-membrane. In it, besides the fibrin, are found pus cells, des-

quamated epithelium, bacteria, and sometimes a few red cells. This membrane is grayish in color, tough, and when removed leaves a raw bleeding surface.

It may occur as an extensive layer over the larynx or in isolated areas. It may be removed, but reproduces very rapidly.

Although a pseudo-membrane is more commonly caused by the diphtheria bacillus, it may result from streptococci or from the action of irritating vapors.

Tuberculosis of the larynx is quite common as a primary lesion, usually being an infection on top of a chronic inflammation. May be secondarily infected by tuberculous material from the lungs. It generally appears in the form of scattered miliary tubercles which frequently break down and ulcerate. This occurs rapidly on the vocal cords. The lesions are most common about the posterior commissure, the arytenoid cartilages, and the true vocal cords, seldom on the epiglottis.

The ulceration may be very destructive, involving the submucosa and even the cartilages, causing inflammation and necrosis of them.

The larynx may be the seat of the slowly spreading form of tuberculosis known as lupus.

Syphilis may be either of a mild or a very severe type, the commonest form being a simple catarrhal laryngitis with infiltration of the mucosa and submucosa. Gumma may form in the submucosa, break down, and give rise to extensive ulceration, with perichondritis and necrosis. As the healing processes go on, large amounts of fibrous connective tissue are formed. These undergo contraction with frequently marked deformity, greatly interfering with speech.

Leprosy gives rise to nodular lesions, quite similar to what may be found in syphilis. They break down, ulcerate, and in healing form large scars.

Glanders is rarely found. In it there is a cellular infiltration with the formation of suppurating ulcers.

Foreign bodies of various sorts may gain entrance and become lodged in the larynx.

Tumors.—The most common tumors are the *papillomata*. They vary greatly in size and shape and the greater number are of inflammatory origin. They consist of a more or less dense framework of fibrous tissue covered by a layer of epithelium. These growths may be quite flat and but little raised above the surrounding surface, or they may be distinctly polypoid. The fibrous tissue may show mucous changes, and the glandular structures be distended with secretion, so as to form cyst-like growths.

Small *fibromas* are sometimes found. *Adenomata* are rare.

Malignant tumors may occur; of these, the *sarcoma* is very rare. When present, it does not involve the cervical lymph-nodes. The *epithelioma* is more common and may arise from either the vocal cords and ventricles or from the arytenoid folds and the epithelium covering the cartilages.

DISEASES OF THE TRACHEA AND BRONCHI

Malformations of the trachea usually consist of a fistulous opening, the result of failure of closure of the third or fourth branchial cleft. Generally appear along the anterior border of the sternomastoid, a little above the clavicle.

The trachea is the seat of inflammatory processes secondary to those in the neighboring portions of the respiratory system, the larynx, and the bronchi.

Bronchitis may be either acute or chronic. When severe it may extend to the capillary bronchi and involve the adjacent lung tissue, giving rise to an important form of broncho-pneumonia. In the acute variety the mucosa becomes congested with swelling, and in the beginning secretion is decreased. There is soon an increased exudation, at first thin and with but few pus cells, but soon becoming thick and tenacious and containing more cells. There is a desquamation of the epithelium and the walls will show a round cell infiltration.

If there is much expectoration of a serous type the condition is known as *bronchorrhea serosa;* if purulent in character, *broncho-blennorrhea*. Blood may be present as a result of congestion or rupture of capillary vessels,

The cause of bronchitis is not definitely known. It is probably bacterial in origin, but it commonly follows exposure to cold which lowers resistance against infection.

Chronic bronchitis may follow repeated acute attacks or accompany various chronic diseases of the lung or heart, particularly in those in which there are marked circulatory disturbances. The mucosa is much congested, the secretion may be scant or plentiful, and there may be distinct projections on the walls. The epithelial cells may undergo hyperplasia or atrophy. Instead of proliferative changes there may be atrophy with weakening of the bronchial walls and dilatations.

Fibrinous bronchitis is a condition in which a small area of the terminal bronchi and bronchioles are involved. It is marked by the expectoration of a dense yellowish-white substance moulded in the shape of the air-passages from which it came. The larger stalk is usually hollow, the smaller branches being solid and the walls commonly laminated. Although resembling fibrin it does not always give the characteristic reaction and may be evidently inspissated mucous. In the meshes of the bronchial cast are leukocytes, broken-down epithelium, and Charcot-Leyden crystals such as are found in asthma. Curschmann's spirals are also found. These are collections of fine fibrils twisted like a corkscrew. They are present at the end of the smallest branches of the cast.

In diphtheria and in croupous pneumonia there may be the formation of a true fibrinous exudate. The mucosa of the bronchi is reddened and is more or less completely covered by a pseudo-membrane.

Bronchiectasis, or dilatation of a bronchus, may follow chronic bronchitis in which there has been atrophy and weakening of the bronchial wall, or it may be due to an increase in the air-pressure. The medium-sized bronchi of the lower and middle lobes of the right lung are the ones most frequently involved. The enlargements are usually saccular, but may be fusiform or cylindric. There may also be several in the course of a single bronchus. The walls may appear of normal thickness, but this is due to fibrous tissue formation, as

the normal tissues are atrophic, particularly the mucous membrane.

In fibroid phthisis the contraction of the new formed fibrous tissue may drag upon the bronchi and cause them to dilate.

The walls of the cavity may be smooth, lined with epithelium and may contain remnants of the normal bronchial wall. If the cavity be roughened by ulceration it will be at the most dependent point as it is there that the retained secretions will act.

FIG. 139.—CHRONIC FIBRINOUS BRONCHITIS.
Fibrinous Casts of the Bronchi, Similar to those Shown in the Photograph, were Coughed up at Irregular Intervals for Several Years (Delafield and Prudden).

The openings of entrance and exit may be evident. There will be no shreds of blood-vessels, or of other bronchi or bronchioles present.

As the walls become weakened, secretions in large amounts may be retained and by their weight cause extensive bronchiectasis. The various dilatations may, on account of atrophy of the intervening tissues, communicate. They may be filled with secretion, with cyst formation resulting. The wall of the cavity is, as a rule, smooth or only slightly granular.

This material may undergo decomposition with subsequent gangrene or it may dry up.

Obstruction of a bronchus may be the result of inflammatory changes within the wall, of tumors or foreign bodies inside, or of pressure from the outside.

Foreign bodies more commonly lodge in the right bronchus, and may cause ulceration and pneumonia or gangrene of the lung.

Ulceration of the bronchi may follow acute or chronic bronchitis, or be due to the presence of foreign bodies. The most common cause of severe ulceration is tuberculosis. The lesion may be superficial or so deep as to cause necrosis of the cartilage with perforation of the bronchus. In such a case the material may escape into the lung and cause suppuration.

Tumors.—Primary growths are uncommon, but secondary tumors are more frequent, particularly carcinomata.

DISEASES OF THE LUNGS

Circulatory Disturbances

Anemia of the lung seldom occurs. Is due to pressure causing vascular obstruction.

Acute hyperemia or congestion may be caused by the inhalation of irritating gases or it may be collateral, due to obstruction in some other part of the lung. It is also the first stage in inflammations of the lung. The organ is dark red in color; on section blood escapes from the cut surface. The tissue will float in water.

Chronic or *passive hyperemia* is generally due to obstruction of the pulmonary veins, and is associated with disease of the aortic and mitral valves and a weakened and relaxed condition of the vessel walls. The dependent portions alone may be involved—*hypostatic congestion.* This predisposes to infection and may terminate in hypostatic pneumonia.

The lung in passive hyperemia is dark red in color, firm, and crepitation is less than normal. From a cut surface there escapes on pressure a frothy purplish fluid. Resulting from the congestion, there is frequently proliferation of the fibrous connective tissue, giving rise to *cyanotic* or *brown* induration of

the lung. The air vesicles will contain leukocytes, red cells and desquamated epithelial cells. These latter frequently contain hematogenous pigment, resulting from the destruction of the erythrocytes. This form of hyperemia is frequently seen post-mortem.

In *edema* of the lung there is an escape of serous fluid into the bronchi and air-vesicles. Is generally found as a result of chronic congestion following heart and kidney disease, but may follow the inhalation of very hot or very cold air, or be part of a general angio-neurotic edema. Is very frequently found as a terminal affection in many diseases. The lung may be either pale or dark, according to the amount of congestion present. Is heavy and boggy, but crepitates, and from the cut surface a thin, frothy serum escapes in large quantities.

Hemorrhage from the lung, or *hemoptysis*, occurs in many conditions—trauma, embolism, etc.—but is most common in phthisis, particularly in the later stages when ulceration has taken place. The blood may be expectorated or part of it may enter portions of the lung. These areas do not contain air, are dark in color, and resemble splenic tissue.

Hemorrhagic infarction is merely a localized hemorrhagic area following obstruction of the arteries by emboli. It will not occur, as a rule, unless passive congestion or some other circulatory interference is present. The area is usually just beneath the pleura with its base circumscribed and directed outward, the apex directed toward the hilum; is dark red, almost black in color, dense and airless. The air-spaces and the inter-alveolar tissues are filled with erythrocytes and some fibrin. Infarcts may be small or large, single or multiple. If infection does not take place the tissues may regain their normal condition. Usually there is degeneration with subsequent cicatrization, an irregular depressed scar resulting.

Atelectasis or collapse of the lung may be either congenital or acquired. The *congenital* or fetal form occurs in newborn babies who have never breathed, either on account of an obstruction to a bronchus or from lack of strength. The entire lung or portions only may be involved. Obstruction

of the upper air-passages by meconium or amniotic fluid will cause atelectasis.

The *acquired* form develops after expansion has once taken place, and may result from pressure from the outside, as in pleuritic effusions, neoplasms, etc., or it may follow obstruction of a bronchus with absorption of the contained air, the vesicles then collapsing. The involved area varies in color, according to the amount of blood present, from a pale red to a dark brownish color. The lung will be pale when the atelectasis is due to pressure from the outside. The tissue is dense, dry, tough, does not contain air, and will not crepitate; will sink when placed in water. If there is much congestion, the tissue looks like meat and the condition is termed *carnification.* If the atelectasis has existed for some time, there is proliferation of fibrous connective tissue, giving rise to an appearance resembling the spleen, known as *splenization.* Inflammation, with fibrosis and the deposit of lime salts, may occur in the involved area.

Emphysema is a condition of overdistention of the air-cells with an increased amount of air present in the lung. It is due either to a loss of elasticity of the air-cells, to an increase in the air-pressure, or to both. Is frequently due to violent expiratory efforts in coughing. In *interstitial* emphysema there is rupture of the air-vesicles with the entrance of air into the interlobular tissue of the lung, small bubbles appearing beneath the pleura. These change place on pressure.

Acute vesicular emphysema results from forced inspiration. In it there is merely overdistention of the vesicles without structural alterations.

In *hypertrophic* or *substantive* emphysema there is extensive and permanent dilatation of the vesicles. Is generally found in those who suffer from chronic bronchitis and in glass-blowers or players of wind-instruments, the important factor being obstruction to the expiration. It probably rarely or never occurs in lungs that are not congenitally weak on account of a loss of elastic tissue. The lung is much increased in size, pale in color, and feels like cotton, the anterior edges being specially involved. The affected areas, although not

edematous, will pit on pressure on account of the loss of elasticity. The loss of color is due in great measure to an actual disappearance of pigment. The edges are rounded, particularly anteriorly and at the apex. The vesicles may be so enlarged as to be visible to the naked eye.

Microscopically the vesicles are seen to be greatly enlarged, and the walls much thinned. The elastic tissue fibers lose their

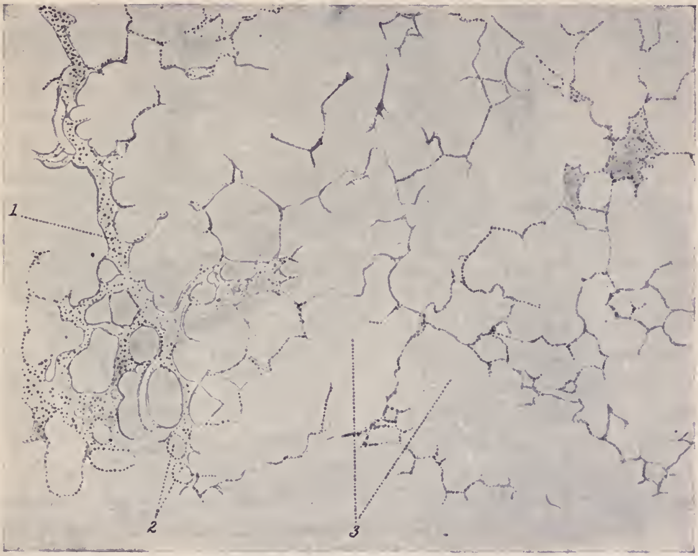

FIG. 140.—EMPHYSEMA OF THE LUNG. 40 × (Dürck).

Greatly dilated alveolar spaces, extraordinarily thin alveolar septa, deficient in cells and torn at many places so that the several alveoli communicate with one another. 1, Interlobular septum; 2, contiguous but normal alveoli; 3, dilated and confluent alveoli.

wavy outline, become swollen and often undergo fragmentation. In many places rupture of the walls may be seen with the formation of one large alveolus from several smaller ones. The ends of the broken septa will extend into the enlarged vesicles. As the walls are stretched the capillaries become narrowed and may finally be completely obliterated. As a result nutrition is interfered with and degeneration and atrophy follow.

In this form of emphysema the chest is barrel shaped. The pulmonary circulation being interfered with, enlargement of the right heart with general venous congestion ensues.

Senile emphysema is that occurring in old age from atrophy of the intervesicular septa. The lung is smaller than normal and frequently accompanied by edema, congestion or even infarction. *Vicarious* emphysema is that found in one part of the lung as a result of obstruction in some other portion. The uninvolved portions of the lung in bronchopneumonia may show a temporary dilatation.

Pneumonia

Pneumonia, or *inflammation* of the lungs, can be divided into various forms according to the nature of the inflammatory exudate, to the mode of entrance of the etiologic material, and to the portion of the lung involved. *Fibrinous* pneumonia when the exudate into the air-sacs and bronchioles is rich in fibrin; *catarrhal* when the exudate contains an albuminous fluid in which are desquamated epithelial cells and erythrocytes; *purulent* when pus cells are numerous; *caseous* when there is cheesy necrosis, and *fibrous* when there is extensive fibrous connective-tissue formation.

It may be *lobar* or *lobular*.

Aërogenic when the infecting substance is conveyed by the air through the bronchi; *hematogenic* when carried by the blood; *lymphogenic*, by the lymphatics; *pleurogenic*, by extension from the pleura.

Inspiration pneumonia, when a large amount of infecting substance gains entrance by the bronchi.

Hypostatic, when the blood, on account of weakened circulatory efforts, settles in the dependent portions of the lung and consolidation takes place.

Pneumonias may also be *acute* or *chronic*.

Lobar, fibrinous, or **croupous pneumonia** is an acute infectious disease, generally caused by the diplococcus of Fränkel. Although usually primary it may follow in the course of other infectious diseases. It usually involves one or more lobes, an

entire lung, or rarely both lungs. It is characterized by an exudation, rich in fibrin, into the air-spaces and bronchioles.

Morbid Anatomy.—The lower lobe of the right lung is most frequently first involved, then the lower left, the apices seldom primarily. An entire lobe is generally involved.

The course of the disease can be best studied by arbitrarily dividing it into three stages—that of *congestion*, of *red* and

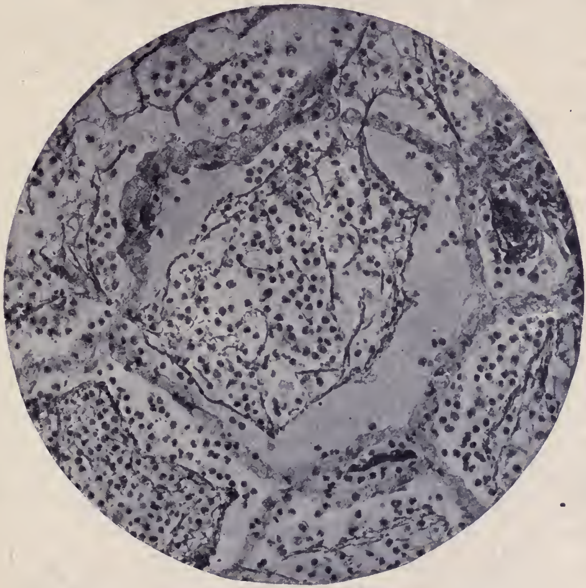

FIG. 141.—LUNG. LOBAR PNEUMONIA (Mallory).
Alveolus filled with an exudation of serum and polymorphonuclear leukocytes. Much fibrin has formed. At two points it runs through openings in the alveolar wall.

gray hepatization, and of *resolution*. It must be remembered that all of these conditions may be present in one lung at the same moment.

Stage of Congestion.—The lung is actively hyperemic, dark red in color, enlarged, and firm. Unlike the healthy lung it is very friable and contains but little air. The air-vesicles are

filled with fluid in which are found pneumococci, numerous red cells, a few leukocytes, epithelial cells, and bacteria. The capillaries are greatly distended.

Stage of Red Hepatization.—In this the exudate has undergone coagulation and there is complete absence of air from the involved area. The lung is solid and resembles the liver in consistency. It may weigh as much as 1500 to 2500 gm. Is swollen, dark red in color, and pits on pressure. From the cut surface, which is quite dry, there project minute plug-like bodies formed largely of fibrin, leukocytes, red cells and epithelium, which give a granular appearance to the tissue. They are formed by the coagulated exudate in the alveoli being pushed outward by the contraction of the elastic fibers. The pleura generally shows some fibrinous exudate. Microscopically the air-vesicles are seen to be filled with red cells entangled in a network of fibrin; leukocytes and epithelial cells are also present. The capillaries are less prominent. The diseased tissue will sink when placed in water. The expectoration in this stage is blood-streaked, or rusty.

Stage of Gray Hepatization.—With the beginning of this stage recovery is indicated. The red cells lose their hemoglobin, the exudate softens and the lung becomes gray or yellowish. This is shown microscopically to be due to changes taking place within the alveoli. The blood-supply being interfered with, the exudate undergoes fatty degeneration, probably due in large part to the greatly increased autolytic processes. The erythrocytes have broken down, the fibrin has disappeared in part, and leukocytes are now present in great numbers. The exudate no longer closely adheres to the walls, but leaves space for the entrance of air.

Stage of Resolution.—The broken-down exudate is removed by absorption and by expectoration, which is no longer rusty, but is purulent. The leukocytes also carry off much of the débris. The lung becomes more moist, is less solid, and crepitation returns. The epithelium of the alveoli and bronchioles proliferates and the lung returns to the normal. There is sometimes a delay in the return of the normal elasticity of the alveolar walls.

Instead of the lung returning to the normal various complications may arise. Infection by pyogenic bacteria may take place, with abscess-formation. Gangrene may also follow, particularly if the circulation is weak. Resolution may be delayed and proliferation of connective tissue occur, giving rise to *fibrous pneumonia*. Microscopically there is seen an extensive cellular infiltration and proliferation. The septa become much thickened and masses of connective tissue extend into the air-vesicles. In alcoholics there is a marked hemorrhagic tendency.

There may be serious conditions associated with lobar pneumonia. The uninvolved portions may be emphysematous and congested, and sometimes edema develops. The infecting organism may gain entrance into the blood and cause inflammations of the serous membranes, particularly endocarditis, pericarditis or meningitis. Cardiac disturbances may occur, probably due to the action of toxins. There is also usually some involvement of the kidneys. Leukocytosis is generally marked. Tuberculosis may follow the pneumonia.

The symptoms in this disease would seem to depend more upon a toxic condition than upon mechanical obstruction to breathing by the filling of the alveoli. This would seem to be shown by the fact that on the fall of temperature, the crisis, the alarming objective symptoms subside. Yet a physical examination made at that time shows no changes in the lung itself.

Death may result from the action of the toxins, from overburdening of the heart, or from some of the associated conditions, as edema or gangrene.

Catarrhal pneumonia or bronchopneumonia is an inflammatory condition of localized areas of the lung resulting from inflammation of the terminal bronchioles, capillary bronchitis. Is also known as *lobular* pneumonia, on account of involving lobules of the lung. Occurs generally in young children and old people. It is due in the majority of cases to infection, and is most common as a sequel to the infectious fevers that are accompanied by bronchitis, as in measles, whooping-cough, and influenza. The diplococcus of Fränkel is the most common

organism but is usually associated with other bacteria. It also follows the inspiration of particles of septic matter, *aspiration pneumonia.* If there has been hypostatic congestion to predispose, *hypostatic pneumonia* may arise from the entrance of infectious particles.

In bronchopneumonia both lungs are generally diffusely involved, areas of consolidation being scattered throughout. In the non-pigmented lungs of children these areas are quite conspicuous. On the pleural surface small nodular elevations, dark red or slightly reddish-gray in color, are seen. Are smooth on section, and are usually surrounded by a narrow zone of congestion. These areas are firm, and when separated from the surrounding tissue will sink in water. The lung in the immediate vicinity may be emphysematous, other portions being collapsed—atelectasis. Microscopically the alveoli are found to contain an exudate, albuminous in character, in which desquamated epithelial cells, leukocytes, and erythrocytes are present. It is seldom that much fibrin is found. There is also a marked round-cell infiltration of the septa. The red blood-cells and the leukocytes are not, as a rule, found in large numbers unless the infection has been due to pyogenic organisms. The exudate may then be hemorrhagic or purulent; in either case gangrene may develop.

The small bronchi are usually inflamed and filled with an exudate similar to that in the air vesicles.

The lung returns to its normal condition through fatty degeneration of the exudate with absorption and expectoration.

Fibrous pneumonia is a chronic condition of the lung resulting from long-continued irritation and is characterized by an overgrowth of fibrous connective tissue in the walls of the alveoli. It may be divided into several forms according to its origin: (1) Pneumonokoniosis, those due to the inhalation of irritating particles; (2) those secondary to the acute pneumonias, chronic congestion or atelectasis; (3) pleurogenic, arising from chronic pleurisy; (4) those in which there is peribronchial and perivascular connective-tissue formation.

Pneumonokoniosis is a condition of the lung characterized by the presence of dust particles of various kinds. When

the fine particles gain entrance, they cause a catarrhal inflammation of the alveoli. Much of the dust may be expectorated, but some penetrates the interlobular connective tissue, where it may remain or be carried to the lymph-nodes. By acting purely as a mechanical irritant, or particularly if the particles are not aseptic, a productive inflammation with the formation of fibrous tissue results. This occurs in both lung and lymphatic tissue.

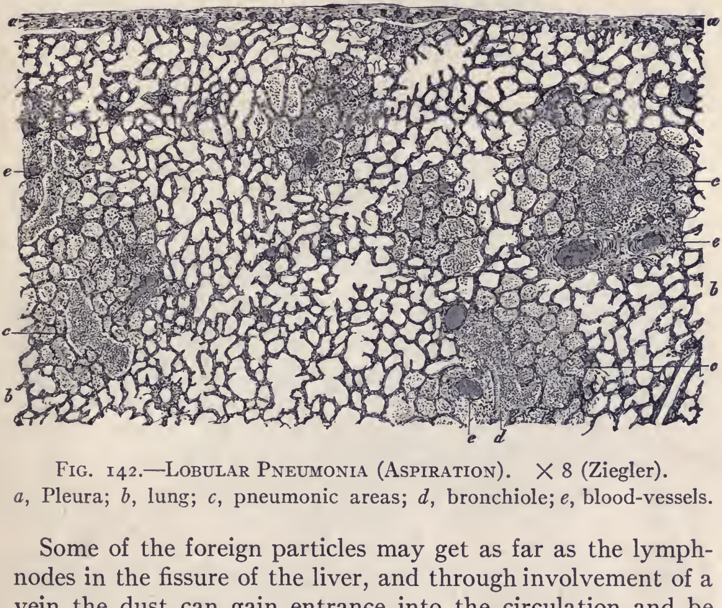

FIG. 142.—LOBULAR PNEUMONIA (ASPIRATION). × 8 (Ziegler). *a*, Pleura; *b*, lung; *c*, pneumonic areas; *d*, bronchiole; *e*, blood-vessels.

Some of the foreign particles may get as far as the lymph-nodes in the fissure of the liver, and through involvement of a vein the dust can gain entrance into the circulation and be deposited in the liver and intestine.

From the irritation a lobular pneumonia may occur and even cavities (non-tuberculous) form. There is always found at post-mortem some dust inhalation, the amount depending upon the environment of the individual.

According to the kind of particles inhaled, the condition receives various names: *Anthracosis*, when coal-dust; *siderosis*, metal dust; *chalicosis*, stone dust.

Secondary fibrous pneumonia results from an overgrowth of the connective tissue of the septa, which become much thickened. There is also proliferation involving the alveolar exudate.

The *pleurogenic* form of fibrous pneumonia results from chronic pleurisy. The lung shows numerous large and

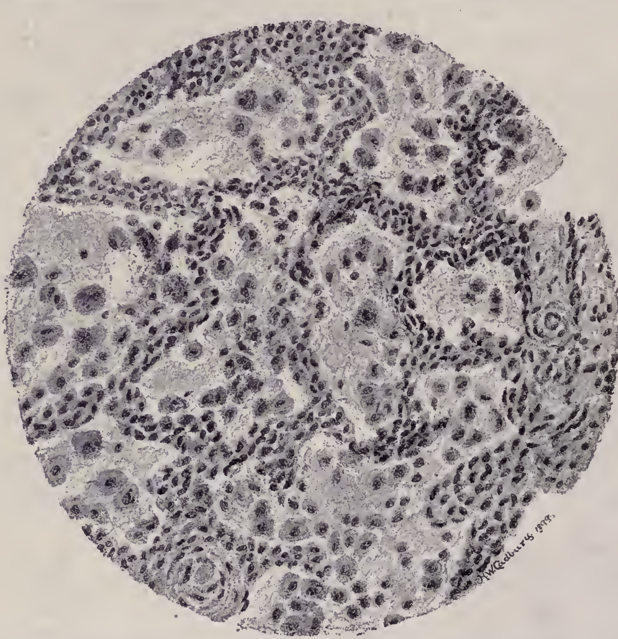

FIG. 143.—CATARRHAL PNEUMONIA, SHOWING DESQUAMATED EPITHELIAL CELLS IN THE ALVEOLAR SPACES (McFarland).

thickened trabeculæ of fibrous tissue extending from the surface deep into the interior of the organ.

The *peribronchial and perivascular* forms present an overgrowth of connective tissue in varying degrees, about the bronchi and vessels. A moderate form of this is found in all the varieties of fibrous pneumonia.

Pleurogenic pneumonia is a form that has its origin in an

inflammation of the pleura. Involvement takes place not only by contiguity but by extension into the deeper portions of the lung by way of the lymphatics—purulent lymphangitis. Abscesses of the lung may be caused in the same way by an extension of an empyema. The lobules of the lung may be separated by bands of suppurating tissue (dissecting pneumonia). There is thickening of the surface of the lung and of the pleura due to an extensive round-cell infiltration.

Purulent pneumonia is one caused by pyogenic organisms. In it there is found a purulent and hemorrhagic exudation, both in the alveoli and fibrous septa. The infection may take place through the bronchi, *bronchogenic;* the blood, *hematogenic;* or through the lymphatics of the pleura, *pleurogenic.*

The *bronchogenic* variety is most marked in the aspiration pneumonias that follow suppurative lesions of the upper air-passages. Large and small purulent collections are found, both in the alveolar walls and within the alveoli as well.

The *hematogenic* form is secondary to purulent areas in other parts of the body. The infectious agents gain entrance into the circulation, and as emboli are carried to the capillaries of the lung. Becoming lodged they set up secondary suppurative changes. Hemorrhagic infarctions are frequently found. The central part is necrotic, while around it is found a zone of severe infiltration. The entire area may soften, break down and form cavities. The abscesses quite frequently evacuate into a bronchus or sometimes into the pleural cavity, giving rise to *empyema*, a purulent pleurisy. Gangrene of the lung may occur.

Gangrene.—This follows the entrance of saprophytic organisms into lung tissue that has undergone degenerative changes. The primary necrosis may follow in the course of pneumonia, tuberculosis, embolism, and infarction. May also result from the aspiration of putrefactive material, as in gangrene of the larynx, foreign bodies in the bronchi; extension of disease of neighboring tissues, as in carcinoma of the esophagus with perforation.

A so-called *idiopathic* form occurs in alcoholics and in asthenic states. Is probably due to infection.

The involvement may be either *diffuse* or *circumscribed.* In the latter, there are usually numerous irregular areas of a dark brown, greenish, or black color. They are rather dry, and are surrounded by a zone of congestion and edema.

In the diffuse variety the condition is much more severe. It may follow the circumscribed form or occur primarily. The gangrene is of the moist variety, the affected area being soft, mushy, greenish in color, and having an extremely foul odor.

The broken-down tissue may be expectorated and leave a cavity through which blood-vessels and bronchi may pass. Generally the vessels are obliterated by means of an arteritis with thrombus formation. The artery may, however, be destroyed before such a protective measure has taken place and severe hemorrhage result.

General embolism with septicemia frequently occurs. If recovery follows the disappeared necrotic tissue is replaced by connective-tissue hyperplasia.

The sputum in gangrene of the lungs is extremely offensive and tends to separate into layers—an upper frothy one, a middle, yellowish and fluid, and a lower layer that is brownish and purulent. In the sediment are found particles of elastic tissue, lung tissue, triple phosphate crystals, margaric acid, pus cells, pigment, and fat drops. Numerous organisms of various kinds are also present.

Tuberculosis

Is caused by the tubercle bacillus and may be either a local disease or a part of a general involvement. The infection may gain entrance to the lungs in three ways: by the air, *aërogenic* or *bronchogenic;* by the blood, *hematogenic;* or by the lymph-channels, *lymphogenic*. All three methods are finally closely associated.

Aërogenic Tuberculosis.—The tubercle bacilli gain entrance by adhering to dust particles or by "droplet infection."

In this latter the fine spray from sneezing or coughing will contain many bacilli and may be inspired by anyone within a range of several feet. They pass down the bronchi, finally becoming lodged upon the mucous membrane of either the air-vesicles or the terminal bronchioles. The apex of the lung is the portion generally involved at first. The bacilli act upon the mucosa as an irritant and set up a mild catarrhal inflammation. The alveoli become filled with desquamated epithelium and leukocytes. This constitutes the primitive tubercle. In it there is a central zone of degeneration a median zone in which epithelioid, giant and round cells, as well as bacilli, are present, and a peripheral zone which contains many round cells but few epithelioid. The bacilli may grow in the air-cells or may be carried by the leukocytes into the lymphatics, so that the original tubercle may be either *alveolar* or *interstitial*, or, if around the bronchi, *peribronchial*. As the organisms increase in number there is an increase in the extent of the tubercle, thus involving neighboring alveoli. These undergo the same changes as the one originally infected. As this process extends there is destruction of the capillary vessels in the tubercles, and as no new ones are formed, there is a loss of nutrition. As a result there is coagulation necrosis of the central part of the tubercle. While this is taking place there is a proliferation of the fixed connective-tissue cells in the structures surrounding the diseased area; round-cell infiltration also occurs.

The tubercle, as it increases in size, approaches and coalesces with neighboring ones till large areas form. The central portion, showing coagulation necrosis, finally opens into a bronchus, escapes, and leaves a ragged cavity behind. Blood-vessels will be exposed, and if destruction occurs before obstructive endarteritis takes place there will be hemorrhages of varying degrees of severity. The blood that does escape furnishes an excellent culture media for saprophytic bacteria. The bronchus may be evident or its walls may have been completely destroyed.

When communication has been effected between a tuberculous focus and the outside air secondary infection by pyogenic organisms occurs. At the same time the tubercular

material is carried along the bronchi during the respiratory acts and other foci are established. The lymphatics carry the bacilli into other parts and there is also involvement of the blood-channels. Consequently all three methods of infection are being made use of and the entire lung may become converted into one mass of broken-down caseous material.

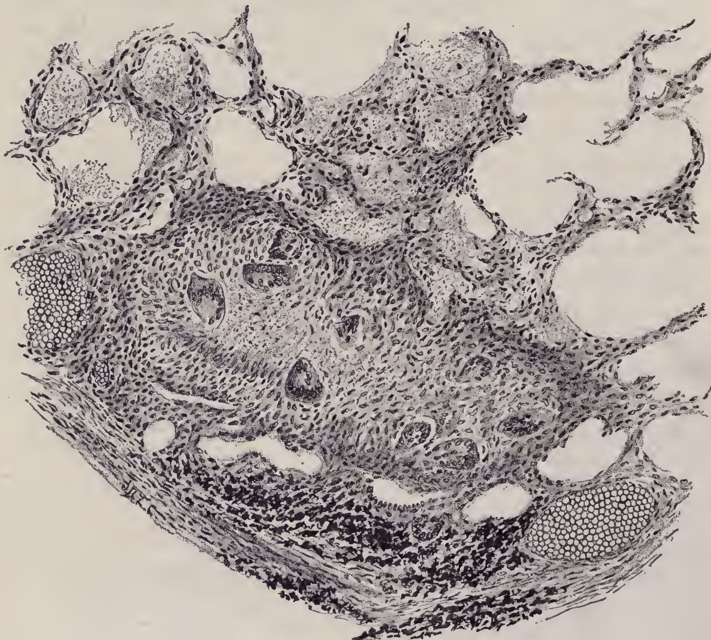

FIG. 144.—PERIBRONCHIAL TUBERCLE OF THE LUNG AND CASEOUS PNEUMONIA OF THE ADJACENT ALVEOLI (Stengel).

In the bronchogenic form the caseation is particularly marked, while in the hematogenic and lymphogenic the involvement is more distinctly miliary. Of the caseous, three different forms are described: The *acute caseous* or *galloping* phthisis; the *chronic ulcerative*, and the *fibrous* or *fibroid* type. This is not an accurate clinical division, as all three processes may be present in the same lung.

Acute caseous tuberculosis, *caseous bronchitis,* occurs most frequently in children. The process is usually quite rapid in this form and the lung resembles somewhat closely the stage of gray hepatization of croupous pneumonia. The infection is at first lobular, but by extension may involve an entire lobe. Either the base or the apex is the seat of the primary focus.

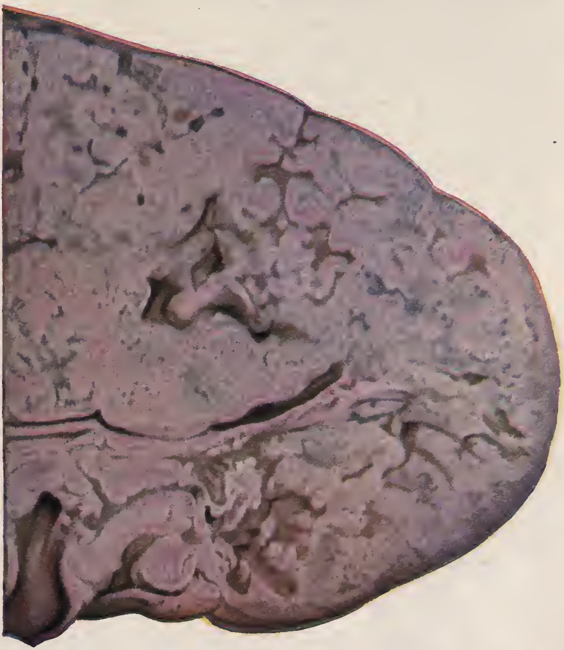

FIG. 145.—SUBACUTE CASEOUS (TUBERCULOUS) PNEUMONIA (Bollinger).

The cut surface of the lung will show irregular yellowish caseous areas with congestion of the intervening pulmonary tissue. On account of the process being acute there is no cavity formation. If cavities are found they are due to a pre-existing, chronic ulcerative tuberculosis. The yellowish areas when closly examined will be seen to consist of bronchi surrounded by caseous material and more or less filled with the cheesy exudate.

The lumen, as a rule, is very rarely obliterated completely. Numerous small excavations form, but there is little attempt at fibrous formation.

If the infection is less severe, there is less confluence of the degenerated areas, and instead of a general infiltration, scattered patches of caseous pneumonia are seen throughout the lung. There is also more fibrous growth, some of the areas becoming completely encapsulated.

Chronic ulcerative tuberculosis is the form most generally met with. It usually begins in the apices and is characterized by the formation of quite extensive cavities. These result from degeneration and necrosis of the lung tissue. Several cavities may coalesce and form a single large one. A large part of the ulcerative process is due to secondary infection by pyogenic organisms. The inner surface of the cavities is rough and irregular, arteries and strands of lung tissue being present. There is fibrous proliferation in the walls, while in the cavity itself there is a secretion containing broken-down caseous material, pus cells, epithelium, and tubercle bacilli and the organisms of the secondary infection.

The arteries traversing the cavities may be the seat of small aneurysms which may rupture and give rise to a fatal hemorrhage. Hemorrhage does not always result when the blood vessels are destroyed as there may have been an obliterating endarteritis resulting from the inflammation.

The healing processes, although well marked in places, are unable, as a rule, to keep pace with the necrosis, and the patient eventually succumbs.

Fibroid Tuberculosis.—This may occur as an essentially chronic condition or it may follow upon acute processes with cavity formation. Surrounding the caseous areas there is a proliferation of connective tissue with encapsulation and the contained material may become completely infiltrated with lime salts. It may be merely surrounded by a capsule, and if anything should occur that should cause destruction of the enveloping tissue, the caseous material could give rise to acute processes, the activity of the tubercle bacilli not having suffered by their confinement.

The newly formed fibrous tissue is, in a way, of distinct disadvantage, as by its shrinking it causes distortion with diminishment in the size of the lung.

FIG. 146.—TUBERCULOSIS OF THE LUNG (McFarland).
The upper lobe shows advanced cheesy consolidation with cavity-formation, bronchiectasis, and fibroid changes; the lower lobe retains its spongy texture, but contains numerous miliary tubercles.

Hematogenous Pulmonary Tuberculosis.—This form results from the entrance of the infecting material into the blood-stream, and is usually part of a general tuberculosis

of the body, but it may be limited to a single lung. The bacilli lodge in the capillaries in the form of emboli and set up minute foci of degeneration—*miliary tubercles.* These are small grayish areas formed in the same way as tubercles elsewhere. When the lungs are alone involved the condition is called *miliary tuberculosis of the lungs.*

Lymphogenic Tuberculosis.—In this the infection generally results from the bacilli being carried from the lymph-nodes, where they have lodged, into the lung tissue by means of the lymphatics. A tuberculous lymph-node may soften and discharge into a bronchus, a form of secondary aërogenous infection. Extension may occur from a tuberculous pleurisy. In such cases there is frequently associated a suppurative lymphangitis. The processes in the lymphogenic form are quite similar to the hematogenic variety and show tubercle formation.

A patient recovers from tuberculosis when the lung becomes sufficiently immunized to resist further progress of the bacilli. In such cases the tubercles will have been encapsulated by new-formed fibrous tissue, isolated and calcified.

Tuberculosis of the lungs may be complicated by secondary infections elsewhere, particularly of the intestines. This results from the swallowing of the infectious sputum and is most common in adults. The larynx may be involved in the same way. There may be infection of the pleura with the formation of adhesions that can interfere very much with respiration. Lobar pneumonia may involve the non-tuberculous areas of the lung or emphysema may be present. *Pneumothorax* may be caused by the tuberculous process rupturing into the pleural cavity, with collapse of the lung. There is usually an accompanying empyema resulting from the infection of the pleura by the discharged material. *Hemorrhage, hemoptysis,* is the most dangerous and common complication. It may follow the rupture of a small aneurysm or the erosion of a vessel before a thrombus has had time to form. It may be slight or very severe. Some of the blood may remain within the lung and, forming a good medium

for the growth of saprophytic organisms, give rise to gangrene.

The apices are the most common primary seat. This is probably due to the fact that their bronchi come off at such an angle that they are easily obstructed; that on account of being furthest away from the entrance of the blood-vessels they are more poorly nourished, and that the apex undergoes the least distention during respiration.

Syphilis.—This may be either *congenital*, the lungs being involved as well as other parts of the body, or it may be *acquired*.

The congenital is the more common and occurs as *white pneumonia*, a diffuse form resembling bronchopneumonia. The lungs are whitish in color, completely airless, and firm. Microscopically there is a desquamation of the alveolar epithelium, an infiltration of leukocytes, and a connective-tissue proliferation in the interalveolar and interlobular tissues. There is usually some proliferation of the adventitia of the blood-vessels, also of the intima, so that some of the vessels may be completely obliterated.

Gummata may be present in the new-born either alone or associated with diffuse lesions; are sometimes found in adults. They generally occur near the root of the lung, beneath the pleura, and are commonly few in number and more or less circumscribed. They undergo the usual cycle of round-cell infiltration, connective-tissue proliferation, coagulation necrosis, and, in case of recovery, organization. They frequently undergo caseation, and it may be very difficult, if not impossible, to distinguish them from tuberculosis, except by staining for the tubercle bacillus. These areas present the ordinary microscopic appearances of gummata. The blood-vessels, besides showing a thickening and hyaline degeneration, are surrounded by a round-cell infiltration. The caseous material may be expectorated and the cavity be obliterated by the formation of a cicatrix.

Glanders.—This is very rarely found in the lung in man. The Bacillus mallei may gain entrance by inhalation or by the blood, following infection of the skin. In the first form

numerous grayish or yellowish nodules, varying in size up to that of a pea, are found scattered throughout the lobes. They are made up of a mass of round cells and frequently undergo caseous degeneration.

When infection takes place by the blood there is a diffuse purulent infiltration of large areas of lung, with the formation of abscesses and associated hemorrhagic infiltration.

Actinomycosis.—Seldom occurs. It may result from aspiration of the infecting organism, but is more often a secondary condition following actinomycosis of the upper air-passages or of the anterior or posterior mediastinum. There may be a single focus of infection in the form of a cavity containing a thick cheesy and purulent material in which the characteristic yellowish actinomyces granules are present. Numerous communicating cavities may be present. The lesions may be more general and nodular, these nodes tending to undergo central softening. On account of proliferation of the surrounding connective tissue they may closely resemble tubercles.

Tumors.—Primary growths in the lungs are unusual; secondary ones somewhat more common. Of the connective-tissue variety, small *fibromata*, *lipomata*, *chondromata*, and *osteomata* are found. *Primary sarcoma* is more common than the above and probably originates within the peribronchial lymph-nodes as a small round-cell or spindle-cell tumor. May have primary *endotheliomata* of the pleura with extension into the lung.

Secondary sarcoma of the lung is very common. It occurs in nearly every case of primary sarcoma elsewhere. Numerous small scattered nodules are found. These are whitish in color and frequently undergo softening.

Primary carcinoma is very rare, but it may develop from the mucous glands of the bronchi or a squamous epithelioma from the epithelium of the terminal bronchi and alveoli.

Secondary carcinoma is not as common as secondary sarcoma. It results from emboli of tumor cells lodging in the capillaries. May follow extension of an esophageal or mammary carcinoma. Sometimes may have secondary growths

resulting from the inspiration of cellular particles of a carcinoma of the mouth or upper air-passages. Such cases may be associated with areas of bronchopneumonia.

Adenomata have been met with and *dermoid cysts* occasionally appear.

In *leukemia* numerous miliary growths consisting of small round cells may be found. They resemble tubercles except that they are somewhat whiter and softer, but do not tend to undergo caseous changes.

Parasites.—Besides the specific organisms mentioned various vegetable parasites, as the *aspergillus*, the *mucor*, and the *oïdium*, may be met. Are found at times in tuberculous cavities. May give rise to a *pneumonomycosis aspergillana.*

Animal parasites such as the *lung fluke* are sometimes found. It gains lodgment near the root of the bronchi and discharges its eggs into the mucopurulent secretion that it excites. The eggs are found in the sputum. May give rise to hemoptysis. The *cysticercus cellulosæ*, the *strongylus longivaginatus*, *monas*, *cercomonas*, *coccidia*, and *psorosperms*, may all be occasionally found in the lung.

The most important is the *echinococcus*. It is usually secondary to primary disease of the liver and is most common in the lower right lobe. There are one or more cysts which may vary greatly in size. As a rule, the cyst occasions no symptoms, becoming inspissated and calcified. Sometimes it ruptures into a bronchus; in such a case the cystic contents will be expectorated and in the sputum characteristic hooklets can be found. An empyema can be caused by the cyst rupturing into the pleural cavity.

DISEASES OF THE PLEURA

Secondary involvements are more common than primary diseases on account of the relation of the pleura to the lung.

Active hyperemia is an early stage of pleuritis.

Passive hyperemia occurs in diseases in which there is interference with respiration; is most common as a result of venous stasis due to cardiac disturbances. *Hydrothorax* may result from it.

Hemorrhage. If there is extreme congestion petechiæ will be found. Are most marked in death from suffocation, but also occur in diseases of the blood and in hemorrhagic diatheses.

Large hemorrhages may result from traumatism, from rupture of large aneurysms, from fractured ribs, and from malignant tumors.

The blood that escapes into the pleura will not coagulate, as a rule, and is slowly absorbed if it has not become infected. Adhesions will form to some extent.

Hydrothorax is a condition in which both pleural cavities, as a rule, contain a non-inflammatory, watery, straw-colored fluid of a low specific gravity that does not undergo spontaneous coagulation. It occurs in chronic heart and kidney disease as a part of a general dropsy. The pleura is frequently opaque and lustreless and edematous. The lymph-channels are dilated and the endothelial cells may desquamate. From the pressure of the fluid the lungs are pushed backward and may be so much compressed as to interfere greatly with respiration. The lung may be even atelectatic. The effusion may occur suddenly, as in carbon monoxid poisoning, or be very chronic.

Is generally a slight effusion into the pleural cavities just before death.

Pneumothorax is the entrance of air into the pleural sacs. Is the result of accident and is almost invariably followed by infection and empyema. It results generally from the rupture of a tuberculous lesion, from gangrene or abscess of the lung, or from the rupture of an emphysematous air-vesicle. On account of adhesions the perforation seldom occurs at the apex. May be due to perforating wounds of the chest, to the rupture of an empyema into the lung, or from perforation of a gastric ulcer.

With each inspiration air escapes from the lung into the pleural sac until the pressure becomes so great as to seriously interfere with the expansion of the organ. The lung is pushed backward, is much compressed and may be airless. The opposite organ is displaced to one side, the diaphragm downward, and the intercostal spaces bulge.

The air may be absorbed, but as a rule infection occurs, giving rise to a *pyopneumothorax*, a combination of air and a purulent exudate.

Pleurisy or pleuritis is an inflammation of the pleura. It may be either primary or secondary, usually the later, as it most commonly occurs in the course of inflammations of the lung, as in pneumonia, tuberculosis, and gangrene. Also from involvement in inflammatory conditions of the pericardium, of the spine, the ribs or the chest wall. May be the part of a general infectious process, as acute articular rheumatism, or septicemia.

Many micro-organisms have been found, as the streptococci and staphylococci, colon bacillus, tubercle bacillus, pneumococcus and many others.

The involvement may be *local* or *general* and, according to the variety of exudate, *fibrinous*, *serofibrinous*, *purulent*, and *hemorrhagic*.

A single case of pleurisy may pass through all the above stages. In them all the pleura becomes hyperemic, and instead of being smooth and glistening, is rough and dull; the two layers of pleura do not glide with ease and an exudate escapes into the cavity.

In *fibrinous pleurisy* there is soon an exudate of fibrin forming a thin yellowish layer on the surface. It may increase in thickness and cause the pleural surfaces to adhere slightly, giving rise to the so-called "bread and butter" pleurisy. This exudate is composed of flakes and masses of fibrin containing leukocytes. The endothelium below is thickened and in places has desquamated. The sub-endothelial connective tissue is infiltrated by round cells and the vessels are congested. The "friction rub" characteristic of this condition is due to the rubbing together of the two layers of the pleura.

The exudate may be absorbed completely, but if there has been much fibrin formation adhesions of varying density result. New capillaries penetrate the fibrin masses, the fibroblastic cells proliferate, and organization takes place. These bands, although at first delicate, soon become very dense.

They may be so extensive as to cause almost complete

obliteration of the pleural cavity, or be present in scattered areas only. There may be areas on the surface of the pleura of marked chronic thickening.

Serofibrinous Pleuritis.—In this variety there is a large amount of serous exudate as well as fibrinous. It may follow the fibrinous form, but usually begins with a serous outpouring. The fluid is denser than that in hydrothorax, and contains bits of fibrin as well as red and white blood cells in small numbers. The amount of fluid may be very little or as much as several liters. The exudate may become somewhat hemorrhagic if large numbers of erythrocytes are present. The lung is pushed backward and the neighboring organs pressed upon.

Hemorrhagic pleuritis is generally the result of tuberculosis or of malignant disease of the pleura. The exudate is chiefly serous, with red blood-cells present, but at times may be almost pure blood.

Empyema or purulent pleuritis is the result of infection by some one of many micro-organisms. It may begin as a purulent pleurisy or it may follow infection of a sero-fibrinous pleuritis. It may result from some traumatism causing an opening into the pleural sac or occur in the course of disease of the lung. In the adult its cause is most frequently the streptococcus, in children the pneumococcus. Tuberculous infection in adults is nearly twice as frequent as in children. The infecting organism, whatever it is, can be carried to the pleura either by means of the lymphatics or the blood-vessels. The organisms most commonly found are the streptococcus, pneumococcus, tubercle bacillus, staphylococcus and B. pyocyaneus.

In the pleural cavity there is found a small or a large amount of a cloudy purulent fluid which contains great numbers of pus-cells. The color may be at times greenish, although usually yellowish. The pleuræ are generally thickened and congested and covered with flakes of fibrin and degenerated endothelium. The pus may be completely absorbed and the two inflamed pleuræ unite with dense adhesions, or it may become cheesy and undergo calcareous

infiltration. The changes are most marked in the visceral pleura, which becomes greatly thickened and at first is soft and edematous, while fluid is still present. When the exudate disappears it becomes very hard and callous.

During the course of the empyema there is always more or less involvement of the lung. The fluid by its presence tends to push the lung backward and compress it. This may continue till expansion is impossible and atelectasis occurs. There may be an infection with resulting pleurogenic pneumonia. Rupture of the empyema into the lung sometimes happens, in which case the result is generally fatal.

Tuberculosis of the pleura is rare as a primary lesion; is usually secondary to similar disease of the lung or adjacent tissues. The primary form occurs as small, round, pearly bodies about the size of a pea. The pleura may be involved in the course of a general hematogenic infection. Will vary greatly in appearance; many small miliary tubercles in some cases, while in others the pleura may be covered by a widespread exudate. The fluid present may be sero-fibrinous, purulent, or hemorrhagic. It may become inspissated and calcification take place.

Syphilis of the pleura may be present as a part of a general syphilitic infection, but it is unimportant clinically and difficult to recognize at any time.

Tumors of the pleura are not very common, the most frequent variety being the *endothelioma*. It may be present as a diffuse infiltration of the pleura, resembling somewhat old adhesions, or in nodules scattered about. Secondary growths, as *sarcoma* or *carcinoma*, may result by metastasis or by direct extension from malignant disease of adjacent tissue, particularly by extension of carcinoma of the mammary gland through the chest wall. Other varieties found are the fibroma, lipoma, osteoma, and chondroma.

Parasites.—Echinococcus cysts are occasionally found.

CHAPTER XXI

DISEASES OF THE DIGESTIVE SYSTEM

Malformations.—The most common deformities are *cleft palate* and *hare-lip*. The former results from a failure of closure of the hard palate and is usually to one side of the mid-line. Hare-lip is the result of failure of union between the superior and premaxillary bones. May be single or double. The tongue may be either unusually large or small. Lack of development of the symphyses of the lower jaw sometimes occurs.

The *lips* may be the seat of ulcers and fissures and sometimes of a chronic inflammation with thickening.

Anemia of the mucous membranes of the mouth and lips is commonly seen in cases of general anemia and is a well recognized symptom.

Active hyperemia is found in inflammations and as an early symptom in certain infectious diseases. Passive hyperemia occurs in the general congestion of chronic lung and heart disease. Actual bleeding is found in scurvy and purpura and sometimes in the infectious fevers.

Stomatitis.—Inflammation of the mouth results from many causes, but particularly from local infection by bacteria. It differs greatly in severity and is divided into catarrhal, ulcerative, mycotic, and gangrenous forms.

Catarrhal Stomatitis.—This, the commonest form, results from the action of irritants, such as hot liquids, chemicals, tobacco, decaying teeth, or from a depressed condition of the general system. There is marked hyperemia with desquamation of the epithelium. In chronic cases there is frequently a thickening of the mucous membrane with the formation of whitish areas. The mucous glands may enlarge and form small cysts. Associated with the stomatitis there is an increased activity of the salivary glands.

Ulcerative stomatitis is usually found in children who are not well nourished. Occurs in malnutrition, tuberculosis, and in other chronic conditions, also in mineral poisonings, particularly by mercury and phosphorus. Is met with most commonly on the gums, although other parts may be involved. The gums become red and swollen and even hemorrhagic at the junction with the teeth. They become changed into a soft, necrotic mass that bleeds readily. The epithelium is

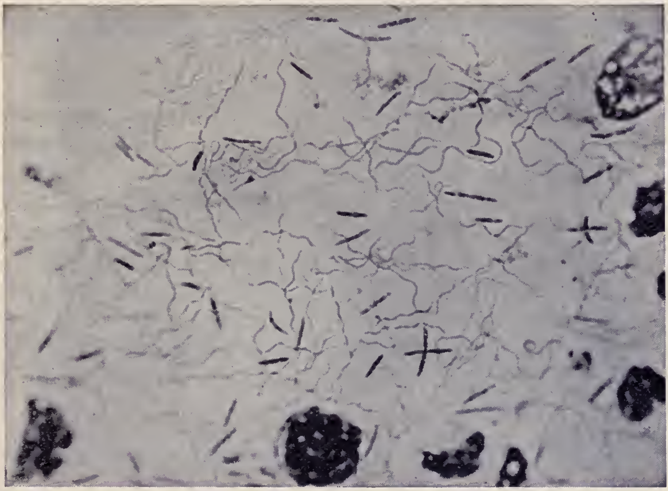

FIG. 147.—SPIROCHÆTA VINCENTI FROM CASE OF ULCERATIVE STOMATITIS (× 1200) (Todd).

destroyed and although the inflammation is usually superficial it may extend and give rise to periostitis, ostitis and even necrosis of the alveolar process. Suppuration may ensue and the teeth become so loosened that they fall out. The inflammatory process may extend to the cheek and the tongue. There is marked increase of saliva, which has a bad odor. Mercury in small doses may cause it in some people who are especially susceptible; is then known as *salivation*.

Mycotic stomatitis is that which is directly due to microorganismal infection. Of this variety the *aphthous* or *follicular*

stomatitis is an example. It occurs usually in children who are in poor physical condition. On the mucous membranes of the mouth there appear small whitish spots surrounded by an inflammatory zone. These areas consist of degenerated epithelium and fibrin, and the condition is therefore sometimes spoken of as croupous stomatitis. Ulceration seldom occurs. The condition may last for some time, the exudate finally being absorbed and the epithelium regenerating.

Thrush is that variety of mycotic stomatitis caused by the *oïdium albicans* which involves those structures covered by squamous epithelium. The tongue is most frequently involved primarily, but secondary infections through contact may develop. Usually occurs in marasmatic infants, but sometimes in debilitated adults. There is at first a diffuse reddening of the mucous membrane, then the formation of patches of a shining, whitish false membrane that adheres at first rather tightly to the underlying tissue, but finally becomes loose. The patches may coalesce, forming large areas of a pseudo-membrane that is composed of desquamated epithelium and parasitic threads. If the membrane is removed it soon reappears. The disease may spread from the tongue to the pharynx and esophagus, and it has been known to extend into the stomach and bronchi.

The oïdium albicans is a budding fungus resembling the yeast and forms long myceliæ. Can be cultivated upon acid media that contain sugar. Longer threads form when grown on an alkaline medium.

Gangrenous stomatitis or *noma* is a rapid necrotic process involving the mucous membrane of the cheek. It occurs in children between two and twelve years of age whose general condition is extremely poor, either as the result of chronic or severe acute disease. Near the angle of the lip on the buccal surface there appears a livid area that rapidly becomes gangrenous. Penetration through to the skin may occur or the process may remain localized in the mucous membrane and underlying tissues. When the skin is involved vesicles are formed and the tissue soon breaks down into a foul-smelling mass. Death from exhaustion and secondary infection usually

follows. The slough may separate and the patient recover, with usually marked deformity from the cicatrization. Although more common in female children, noma may occur in either sex and at any age. This process has been met with in the genital regions.

Syphilitic stomatitis may occur either as the primary chancre or, what is more common, as the secondary mucous patch. The primary form may appear on the lip, tongue, or tonsil in either a soft or an indurated form. Is accompanied by enlargement of the lymph-nodes. The mucous patches are superficial ulcers following cellular infiltration. Other secondary lesions may be present. The epithelium of the mucous membrane may become greatly thickened, *leukoplakia*, and eventually undergo malignant change. *Gumma* are also found either in the corners of the mouth or more commonly on the palate. Are generally small and prone to undergo softening with ulceration and subsequent cicatrization.

Tuberculosis may rarely be primary, but is usually secondary to infection from tuberculosis of the larynx or pharynx or by infected sputum. Usually involves the posterior portion of the tongue, where small nodular tubercles of a yellowish-red color appear. They soon degenerate and form ulcers with thickened edges. The lesions may very closely resemble epithelioma.

Actinomycosis may result from the infection of an abraded surface by the fungus. It generally gains entrance to the alveolar border of the jaw by way of carious teeth. The process is generally a slow one of swelling with destruction of the adjoining tissues. There may be quite widespread involvement of the lymphatic nodes of the neck and jaw.

Glossitis or inflammation of the tongue occurs either in a superficial or a deep form. In the *superficial* variety there is a desquamation of the epithelium. It may follow marked intestinal disorders or be the result of local irritations. The surface of the tongue becomes white or brown, due to the degenerated epithelium, particles of food, and bacteria. May become dry, hard, and fissured. If the superficial glossitis becomes chronic, local thickenings of the mucous membrane

are formed. They are irregular, slightly elevated, whitish patches, which may spread and coalesce. This variety is known as *leukoplakia* or *psoriasis linguæ*. Occasionally the thickened epithelium may desquamate and leave an ulcer. Quite frequently secondary epitheliomata develop at the site of the lesion.

The *deeper* inflammations of the tongue generally result from injury and infection. The organ may become swollen, painful, and infiltrated by leukocytes; small abscesses may also form. Is usually accompanied by some degeneration and atrophy of the muscles.

One form of inflammation of the tongue is known as *melanoglossia*, black tongue. The epithelium upon the papillæ, particularly the filiform variety, becomes greatly increased and gives rise to a hairy appearance. The color may be due to an increase of pigment in the epithelium or to a fungus mixed with which are particles of food and bacteria.

Tumors of all kinds are found within the mouth. Of the connective-tissue forms, *lipoma*, *fibroma*, *myxoma*, and *sarcoma* occur, also *lymphangioma* and *hemangioma*. *Adenoma* and *carcinoma* of the squamous type are found. *Sarcoma* generally appears upon the gums near the roots of the teeth and is known as *epulis;* is generally of the giant cell variety. Some epuli may be pure fibromata. The carcinoma is generally present in the form of the *squamous epithelioma*. Is found most commonly on the tongue at one side, where its course is quite rapid. It frequently occurs at the site of a long-continued ulceration from a carious tooth. It appears as a circumscribed hard swelling which soon breaks down and rapidly ulcerates. It soon involves the neighboring cheek and larynx, and gives metastases to the cervical and submaxillary lymph-nodes, and if excised it soon returns.

Cysts result from obstruction to the ducts of the mucous or salivary glands. A *ranula* is a cystic dilatation of Nuhn's glands situated under the tip of the tongue, which may be displaced backward and upward. A thick viscid fluid fills the cavity. *Dermoid* cysts are also found.

Macroglossia, thickening of the tongue, and *macrocheilia*,

thickening of the lips, result from a lymphangioma. The lymphatic spaces are much distended and contain liquid and round cells. This condition is generally congenital, the result of thyroid deficiency; is met with in cretins.

THE TEETH

Malformations.—They may be unusually large or small, increased or decreased in number, or even entirely absent. In congenital syphilis the upper central incisors of the permanent set are frequently malformed, being deeply notched at the edge.

Inflammation may involve the surrounding alveolar periosteum or the pulp of the tooth. It may go on to pus formation with loosening and death of the teeth. *Caries* is generally the result of malnutrition or lack of care of the teeth. The enamel of the tooth is destroyed by lactic acid, which is formed by many varieties of bacteria. The organisms are then able to enter the canals in the dentin with subsequent disintegration. The tumors of the teeth have been described in Part I.

THE TONSILS AND PHARYNX

Anemia and hyperemia occur here just as elsewhere. Active hyperemia as a beginning of inflammation; passive, in chronic heart and lung disease, in which cases the veins may be distinctly varicose. Edema is found in connection with inflammation and ulceration and may be quite marked. Hemorrhage may occur in purpura and in severe infectious fevers, as well as being the result of direct injury. The blood may form quite a tumor between the layers of the soft palate.

Tonsillitis, or inflammation of the tonsil, may be either acute or chronic. *Acute tonsillitis* may be either symptomatic of various diseases or it may be a true local primary condition as a consequence of direct infection. It is known as *catarrhal*, *lacunar* or *follicular*, and *phlegmonous*. In the catarrhal the tonsils are somewhat reddened, usually as a part of a catarrhal pharyngitis. The lacunar or follicular form is characterized by the presence of many small yellowish-white

spots over the surface of the tonsil. Each spot represents a follicle that has become filled with an exudate made up of degenerated epithelium, and bacteria, as staphylococci, streptococci, pneumococci, and tubercle bacilli. The exudate from the lacunæ may extend over the surface of the tonsil, forming a covering that resembles diphtheritic pseudo-membrane. The exudate within the lacunæ may become inspissated and calcify. If the infection passes through the bottom of the crypts into the deeper tissues phlegmonous tonsillitis may result, usually unilateral. In this there is abscess formation as well as round-cell infiltration. These collections of pus may discharge into the mouth, open into the larynx or even involve the large vessels of the neck, perforation of the internal carotid having occurred.

In *chronic hypertrophic tonsillitis* there is an increase in size of the tonsils, due not only to a hyperplasia of the connective-tissue septa and reticulum, but also to a hyperplasia of the lymphoid follicles. The tonsils may become so hypertrophic as to almost meet in the middle line, and by so doing cause obstruction to breathing and swallowing.

This form is frequently accompanied by marked disturbance of the general health and development. Is often found in children, and as a result they breathe with their mouths open; their digestion is often impaired and their mentality may be distinctly lessened.

Instead of the above hypertrophic form, the involvement may be confined to the lacunæ, which are wider and deeper than normal. They become filled with an exudate that through decomposition can give rise to inflammatory processes in adjacent tissues.

Tonsillitis leptothricia is caused by infection of the tonsils by the Leptothrix buccalis. It usually occurs in the poorly nourished, but may occur in a strong, well-nourished individual. Over the surface of the tonsil are numerous spots covered by a thick, dense, dry, whitish exudate that is composed of masses of threads of the leptothrix. It is firmly adherent to the crypts and is removed with difficulty. It usually involves other portions of the pharynx, but does not

occasion much inflammation of the surrounding tissues. It tends to run a chronic course not yielding readily to treatment.

Tuberculosis of the tonsils is quite common. Is generally primary and involves the cervical lymph-nodes secondarily. From there it may by extension gain access to the lungs and occasion tuberculosis within them. It may also give rise to a secondary involvement of the intestines.

Syphilis of the tonsils may occur as a primary, secondary, or tertiary lesion.

PHARYNX

Circulatory disturbances are usually a part of similar troubles of neighboring tissues.

Inflammation.—The *acute catarrhal pharyngitis* or *angina* may result from exposure to cold, to the irritating action of various substances, as tobacco smoke and dust, or may occur as a part of an intestinal derangement. The mucous membranes become red and swollen with decreased secretion at first. As the process goes on there is frequently an abundance of a thick, tenacious secretion composed of mucus and desquamated columnar epithelial cells. In severe cases true ulcers may form along the posterior wall.

In *chronic pharyngitis*, such as occurs in excessive smokers and in those who use their voice a great deal, the posterior wall and the faucial pillars are particularly involved. There is chronic congestion and the lymphoid collections become hyperplastic, causing slight granular elevations. The secretions become less, as a rule, but may be increased and mucopurulent. The pharyngeal tonsils are usually hyperplastic.

Phlegmonous pharyngitis and *retropharyngeal abscess* follow the entrance of bacteria, usually pyogenic, into the deeper tissues or may result from caries of the spinal column, from diphtheria or scarlet fever. If there is rapid abscess formation there is bulging into the pharynx and rupture may take place. If the process has been slower the pus will extend along the deep fascia till perforation into the posterior mediastinum, bronchi, or esophagus occurs. General septicemia not infrequently occurs.

Syphilitic pharyngitis is common as a secondary symptom, but it has no characteristic appearance that renders it easily recognizable.

Tuberculous pharyngitis is unusual. Is generally secondary to tuberculosis of the lungs. The tubercles ultimately soften, break down and form ulcers of varying extent.

Pseudo-membranous pharyngitis may be diphtheritic or non-diphtheritic.

Vincent's angina is an infection of the pharyngeal mucous membrane due to the presence of fusiform bacilli and spirochæte. They cause the formation of a dense exudate which when removed causes bleeding and discloses more or less extensive ulcerations which are very persistent. At times the uvula and even portions of the hard palate are involved.

The *non-diphtheritic pharyngitis* is generally caused by the streptococcus pyogenes or may result from the action of very irritating substances, as steam or ammonia. The appearance of the pseudo-membrane is, to the naked eye, similar to that of the diphtheritic variety. It is not, however, accompanied by the same constitutional depression, nor is it followed by paralyses.

Diphtheritic pharyngitis is caused by the Klebs-Loeffler bacillus and characterized by a pseudo-membrane that is yellowish or dirty gray in color. The involvement may be limited to a small portion of the pharynx, being most common on the arches of the fauces, or the tonsils and nares as well may be concerned. It may extend even into the esophagus and stomach. This pseudo-membrane is laminated, being composed of fibrin in the meshes of which are desquamated epithelial cells, leukocytes and erythrocytes, and the diphtheria bacilli in great numbers. It is formed by the coagulation of the exudate and by coagulation necrosis of the superficial tissues.

This membrane can be removed, exposing a raw ulcerated surface upon which a new membrane quickly forms. The lymph-nodes near-by may enlarge and undergo suppuration.

The extent of the pseudo-membrane does not denote the gravity of the infection. The severity depends upon the viru-

lence of the particular bacillus that has caused the infection; it is the expression of the intensity of the toxin present. In severe forms it spreads rapidly, and if there is a mixed infection with streptococci, hemorrhage and gangrene may result, as well as secondary abscess formation elsewhere in the body.

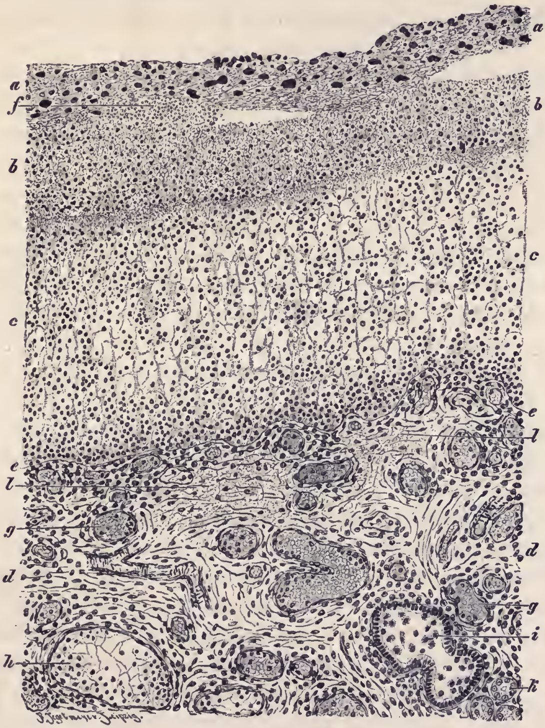

FIG. 148.—DIPHTHERIC MEMBRANE FROM THE UVULA. × 50 (Ziegler).
a, *b*, *c*, Layers of fibrin containing epithelial cells, leukocytes, and bacteria; *d*, *e*, cellular infiltration of the connective tissue; *f*, collections of red corpuscles; *g*, dilated blood-vessels.

Besides the local manifestations there are marked general symptoms due to the presence of a dangerous toxin. The action of this body is seen in the form of small foci of necrosis

in various tissues of the body. Death may result from cardiac paralysis resulting from the presence of the toxin.

Of the internal organs the liver especially shows focal necrosis, in which the cells are degenerated and the nuclei show hyperchromatosis. There is hyperemia of the kidney with cloudy swelling of the epithelium, edema, and hemorrhage. Myocarditis and degeneration of the cardiac muscle also occur. The spleen is also hyperemic.

During convalescence paralysis, particularly of the throat, may occur, also of the muscles of the eyes, the larynx, and the diaphragm. The muscles will show a round-cell infiltration between the fibers and a granular and fatty change of the cells.

There may be degeneration of the ganglion cells of the cord.

Tumors of the pharynx are rare. Squamous epithelioma as a result of extension is the most common, but fibromata and sarcomata have been encountered.

SALIVARY GLANDS

Inflammation of the parotid gland, *parotitis*, or *mumps*, occurs as an independent disease, possibly due to a small diplococcus described by Laveran. The infection probably occurs by way of the parotid duct; the gland becomes much swollen and tense on account of a marked serous exudation and hyperemia. Although abscess formation appears imminent, it is very unusual for suppuration to occur. The exudate can be absorbed and the gland return to a normal condition very rapidly. There may be a chronic induration remaining, or if abscess formation with rupture has taken place, a fistula may result. Secondary inflammation of the testicles, with sometimes subsequent atrophy, or of the ovaries may occur either during the attack or shortly after the inflammation has subsided.

In the inflammation secondary to infectious diseases, as typhoid, scarlet fever, diphtheria, and others, suppuration is not so uncommon. Small abscesses may form and become confluent. The inflammation may become chronic with

hyperplasia of the fibrous connective tissue, or it may subside and leave no traces.

Angina ludovici is a very severe form of inflammation of the submaxillary gland. The infection extends into the surrounding tissues, with suppuration and even gangrene. Abscesses form and discharge either externally or in the mouth; necrosis and gangrene are present and death frequently occurs. Edema of the glottis, with fatal results, may also occur. This disease may be the result of infection by means of carious teeth or infection of the gland itself during the course of an infectious disease, particularly scarlet fever.

Fistulæ of the salivary ducts may follow traumatism or the perforation of an abscess. The parotid duct is the one generally involved.

Concretions or calculi are sometimes found; are called *sialoliths*. They are composed of phosphate and carbonate of calcium, and are found in the smaller as well as the main duct. They frequently give rise to retention *cysts*, the most common variety being that known as *ranula*, a term applied not only to a cystic condition of Nuhn's glands but of the sublingual as well.

Tumors of the salivary glands are not uncommon, the parotid being most frequently involved, the connective-tissue tumors, as fibroma, lipoma, chondroma, and sarcoma, being the most usual. Adenoma and primary carcinoma are unusual. The most common neoplasm is the *mixed tumor* of the parotid. This is composed of sarcomatous tissue, along with cartilage, mucous and fibrous tissue. It grows slowly, does not frequently give metastasis, and when excised seldom returns. It is probably the result of fetal inclusions taking place during the closure of the first branchial cleft.

THE ESOPHAGUS

Malformations.—It may terminate in a blind pouch in its upper portion; it may be double or completely wanting. Fistulæ opening into the pharynx and neck are the result of incomplete closure of the branchial arches.

Circulatory disturbances may be part of a general condition. In diseases of the heart, lungs, and in cirrhosis of the liver passive congestion with varicose veins may be present. Rupture of such veins with severe hemorrhage may take place.

Inflammation of the esophagus, *esophagitis*, may be the result of irritation of foreign bodies, as hot liquids, acids, and alkalies, or of infection. In the *catarrhal* type there is hyperemia, infiltration of the mucous coat, and desquamation of epithelium, with occasional ulcer formation. If the process becomes *chronic*, as in long-continued passive congestion and in alcoholics, the mucous membrane is thickened, and thrown into folds; is dark in color, ulcers are present, and there may be hypertrophy of the muscular coat.

Pseudo-membranous esophagitis may be the result of infection by the streptococcus or by the diphtheria bacillus, or may be caused by swallowing corrosive fluids. It is usually secondary to extension from neighboring tissues that were primarily involved.

Suppurative esophagitis may result from extension of inflammation from the mucosa to the submucous coat, or it may be due to traumatism involving the deeper tissues.

In *smallpox* ulcers may form as a result of the eruption of pustules and *thrush* may extend from the mouth.

Stenosis of the esophagus may be the result of interference from within or from without. *Compression* by tumors, aneurysms, or other lesions. The most frequent cause is a *stricture*, which may take place rapidly or slowly depending upon the severity and extent of the ulceration. This usually results from the contraction of cicatrices formed in the healing of ulcers due to the swallowing of destructive liquids, as acids and alkalies. The commonest site for a stricture is at one of the natural narrowings of the esophagus, at the cricoid, tracheal bifurcation, or diaphragm. May be caused by syphilis, a rare occurrence. Carcinoma may cause stenosis by projecting into the lumen or by contracting the walls. May also be due to obstruction by a foreign body.

Dilatation of the esophagus is the result of an obstruction

and usually occurs at the cardiac end, where it passes through the diaphragm into the stomach. Sometimes dilatation occurs without stenosis, in which case the esophagus is in the form of a pouch, largest at its center.

Diverticula or local sacculations of the esophageal wall may be due to pressure from within, *pressure diverticula,* or to traction from without, *traction diverticula.*

The *pressure diverticula* are more common at the upper part in the mid-line, posteriorly, of the tube, where the greatest pressure occurs. There is loss of tone of the muscular coat and the mucous membrane projects in the form of a pouch from the posterior wall at the pharyngeal junction. They may be very small or as large as a pear. They communicate with the lumen of the esophagus and become filled with food which is retained. This frequently undergoes decomposition, sets up inflammatory changes in the mucosa and adjacent tissues and may rupture.

Traction diverticula are more common and are found near the lower end of the esophagus at the bifurcation of the trachea. They are the result of the contraction of adhesions of diseased bronchial glands, usually tuberculous. Are generally on the anterior wall and are conical in shape with the apex directed outward at the seat of the adhesion. There may be no change in the constituents of the wall, or the muscular coat may be lacking. Perforation may occur if the tension at the apex becomes too great. Escape of the contents may take place into the pleura, pericardium, or lungs. Death may result from hemorrhage following perforation of a pulmonary artery.

Perforation of the esophagus may depend upon causes acting either from within or from without. It may follow from ulcerations caused by the pressure of the cricoid cartilage in bed-ridden patients, or from syphilitic or cancerous ulcers. It may be due to outside pressure from caseating glands, abscesses, gummata, or aneurysms of the aorta. Rupture may be the result of traumatism or be spontaneous. Inflammation to the grade of gangrene may follow the escape of material from the perforated esophagus. If the gastric contents regurgitate there may be a partial digestion of the

walls of the esophagus. This may, however, be a post-mortem condition.

Tumors are not very common, although of the connective-tissue tumors the fibroma, myxoma, myoma, lipoma, and more rarely sarcoma have been observed. The most common growth is the *squamous epithelioma*. It is most frequently found in the lower third at the place where the left bronchus crosses over. The growth is flat, more or less ring-like, and usually ulcerated. The mucous coat is destroyed and papillary projections extend into the esophagus and cause obstruction of the lumen. The submucosa and the muscular coat may become infiltrated and the adjacent tissues also involved. There is stenosis with subsequent dilatation above the tumor. Food is retained and ulceration with perforation may occur, usually into the larger air passages. Metastatic growths are found in the neighboring lymph-nodes, bronchi, pleura, lungs, and liver.

THE STOMACH

Malformation.—It may be completely absent, or abnormally small, with atresia or stenosis of the pylorus, or it may be in the form of two pouches connected by a smaller tube (hour-glass stomach). The stomach may be reversed in its position in transposition of the viscera.

Circulatory Disturbances.—*Anemia* occurs in cases of general anemia, accompanied, if long continued as in pernicious anemia, by fatty degeneration and atrophy of the mucous membrane. The mucosa is thin and frequently smooth. *Active hyperemia* is present normally during digestion, and is widespread. If the result of irritation, the color is more intense and is distributed in irregular streaks or patches, particularly on the tops of the rugæ. *Passive hyperemia* is the result of venous stasis in chronic heart and lung diseases and cirrhosis of the liver. The mucosa is purplish in color, swollen, and edematous. Small punctate hemorrhages may occur and also small erosions. The changes are most marked near the pyloric end.

Hemorrhage of varying severity frequently occurs. This

may be in the form of multiple, minute areas, or as solitary, large lesions. The punctate form, that is found so repeatedly at post-mortems, is in many cases the result of vomiting during the last moments of life. It may also result from congestion and inflammation, or be met with in various infectious and hemorrhagic diseases. If examined carefully, it can generally be seen that over these hemorrhagic points there is a loss of epithelium. The mucosa not being properly nourished at that point is unable to withstand the action of the gastric juice. Particularly as there is no secretion of alkaline mucus to act as a protection.

Massive hemorrhage occurs in destruction of the mucosa in the course of gastric ulcer and gastric carcinoma. In the peptic ulcer the bleeding usually comes from the erosion of a single blood-vessel and may be so great as to cause death. In hemorrhages from this cause and from traumatism the blood is bright red. In the carcinoma there is a slow oozing from degenerated capillaries, with the "coffee-grounds vomit," blood that has been acted upon by the gastric juices. *Melæna neonatorum*, vomiting of blood by new-born infants, is accompanied by the formation of ulcers of the gastric mucosa. It apparently results from imperfect respiration, causing a backing up of the blood. By many it is thought to be due to some cerebral lesion.

Thrombosis of the gastric vessels is rare, but is thought by many to be a cause of peptic ulcer and also of the ulcers that are found in the stomach and duodenum in cases of extensive burns. If infectious, abscesses may occur. *Embolism* is more common; occurs in the course of cardiac disease.

Inflammation or Gastritis.—The *acute* form is generally due to the irritation of certain substances taken into the stomach and is commonly found at the pyloric end. The mucosa is red, thickened, and covered by mucous secretion, and punctate hemorrhages are occasionally present. Microscopically the epithelial cells are found to be the seat of cloudy swelling, numerous goblet cells are present, and there is an infiltration of round cells. There may be considerable desquamation of

the surface epithelium. The lymph follicles are also frequently hyperplastic.

Pseudo-membranous gastritis may be due to the action of caustic substances or to some of the infectious fevers, as smallpox and scarlatina. It may also be the result of the extension of a true diphtheritic process. The mucosa is covered by patches of a grayish-white pseudo-membrane under which the necrotic process may have involved the entire mucosa.

Phlegmonous gastritis is very rare, but sometimes follows the entrance of streptococci. The submucosa and muscularis become swollen and infiltrated by pus cells even to the extent of more or less circumscribed abscesses. These may finally rupture into the cavity of the stomach. Healing takes place by the extension of the epithelium from the neighboring tissues into the opening resulting from the rupture of the abscess.

Chronic gastritis may be the result of repeated acute attacks or it may have been chronic in form from the onset. It follows the abuse of alcohol, results from the eating of too much or improper food, and occurs also in the course of various constitutional diseases. Chronic congestion predisposes, as in cirrhosis of the liver, heart disease and certain lung affections. In the *simple* chronic variety the mucosa is thickened, hyperplastic, and infiltrated, and bands of connective tissue surround projecting areas of epithelium. This is most marked at the pyloric end, where the mucosa may be markedly wrinkled, and is associated with polypoid projections. The stomach is usually larger than normal. *Sclerotic*, *atrophic* or *interstitial* gastritis probably is due to the long-continued action of a mild irritant. There is primarily an increase of the connective tissue, which as it contracts causes atrophy of the glands. The mucosa is very much thinner than normal, grayish in color, and in places there are frequently seen large but slight ulcerations; such a stomach is commonly enlarged. From the contraction of the new-formed connective-tissue stenosis of the pylorus sometimes occurs.

Sometimes there may be a great increase of connective tissue

with a thickening of the walls and a reduction in size of the organ, *cirrhosis ventriculi*.

Peptic or round ulcer is a peculiar form of ulceration generally found in the posterior wall in the lesser curvature at the pyloric end of the stomach, and probably due to the action of the gastric juice upon diseased tissue. It is thought to be due to thrombosis of a vessel giving rise to a local area of necrosis, which, being no longer able to resist the action of the gastric juices, undergoes digestion. Infection, embolism,

FIG. 149.—CHRONIC PERFORATING ULCER OF THE STOMACH (Delafield and Prudden).

infarction, spasmodic contractions of the blood-vessels, are all thought to have some bearing upon the formation of these ulcers. They are found most frequently in chlorotic girls in whom there is an associated increase in the acidity of the gastric juice. The peptic ulcer is usually single and small, but is sometimes multiple and large. It is generally round or slightly oval, 2 to 4 cm., wider at the top than at the bottom, and is accompanied by very little inflammation. The edges are sometimes thickened and raised by an increase of the connective tissue. The mucous layer alone may be involved,

or the destruction may extend to the submucosa, the muscularis, or even to the serous covering. In healing there is cicatricial tissue formed which on contracting gives rise to a peculiar white stellate scar. If the ulcer was in the region of the pylorus, stenosis of that outlet may result. From the floor of the healed ulcer carcinoma sometimes develops. The two dangerous results are perforation or hemorrhage. The perforation is usually smooth and round and looks as if it had been punched out. Sometimes there have been adhesions to neighboring organs, so that damage is prevented, but more frequently the gastric contents will escape into the abdominal cavity and give rise to peritonitis. Hemorrhage is the result of ulceration of a large arterial branch. This is more common than perforation. The amount of blood lost may cause death or there may be merely a constant oozing.

Peptic ulcers sometimes occur in the upper end of the duodenum close to the pyloric orifice and also in the lower portion of the esophagus.

Atrophy of the glands results from chronic inflammation and is also found in old age and in cases of pernicious anemia.

Fatty metamorphosis of the glandular epithelium may follow phosphorous poisoning or occur in the course of severe infectious diseases. The mucous membrane is duller and more yellowish than usual on account of the fat within the cells and interstitial tissues.

Amyloid change is present chiefly in the muscularis, but also to a slight extent in the mucosa. It generally first appears in the walls of the smaller arteries of the submucosa.

Pigmentation of the mucosa is the result of numerous small hemorrhages or occurs as a part of a general discoloration often seen in chronic malaria. The mucosa is of a dark, slaty discoloration.

Calcification of the stomach in small areas has sometimes been found in certain poisonings, such as bichlorid of mercury, that are accompanied by rapid absorption of lime salts from the bones. Particles of calcium carbonate are found in the interstitial tissue.

Gastromalacia is a condition of softening of the stomach

walls due to post-morten changes resulting from the action of the gastric juices. Is most marked when there is hyperacidity and in that part of the stomach that has been most dependent, the portion that contained the stomach contents. If the organ was anemic, the mucous membrane appears pale gray in color and somewhat gelatinous in consistency. If congestion was present, the mucosa will be dark brown. This is particularly marked along the veins, the hemoglobin being transformed into hematin. Sometimes perforation may occur, but this can be recognized readily, as there will be no local inflammatory reaction or peritonitis.

Gastroptosis is a downward displacement of the organ, either acquired or congenital, and is very frequently a part of a general displacing or *splanchnoptosis* of all the abdominal viscera. Is quite commonly due to dilatation following pyloric obstruction.

Dilatation or gastrectasis is usually due to some obstruction, of a chronic character, at the pyloric outlet. Food is retained; this undergoes fermentation and the stomach walls become weaker than ever. This may continue until the organ becomes enormously distended, the mucosa becoming very thin and atrophic. The stomach may be so greatly dilated that the greater curvature will extend not only below the umbilicus, but even down into the pelvis. There may be also a displacement in position, the organ lying almost perpendicularly. Dilatation may also be due to the contraction of adhesions to the outer surface of the stomach.

In some cases, the atonic form, there is a weakening and a relaxation of the walls without any obstruction at the pylorus. In gastrectasis there may be most marked indications of malnutrition.

Acute dilatation, with vomiting of very large quantities of thin fluid, occurs at times shortly after operative procedures of various kinds.

Tuberculosis is extremely rare and **syphilitic** lesions but little more frequent, although gummata may be found. Sometimes a diffuse cirrhosis of all the gastric coats may be found in syphilitics.

Anthrax, actinomycosis, and **glanders** have been described.

Tumors.—The connective-tissue tumors, as *fibroma*, *myoma*, and *lipoma*, have been occasionally found. *Sarcoma* is more rare; it seems to originate within the lymphoid deposits and is generally round-cell in character. Polypoid projections of the mucous membrane are sometimes confused with tumors, but they are not neoplastic, are the result of chronic inflammations, and are sometimes cystic.

Adenomas have been found, but they are unusual, as they generally very quickly undergo a carcinomatous degeneration.

Carcinoma is quite common and is nearly always primary. It is more frequent in men than in women, usually in middle or advanced life. Its most frequent seat is at the pyloric end of the stomach, on the posterior wall of the lesser curvature. It sometimes first appears at the cardiac end. The walls may be more or less involved in the process. The appearance of the growth differs greatly according to its histologic characteristics.

Scirrhus cancer is usually situated at the pyloric opening, which may be completely or partially surrounded. The walls are thickened and indurated. The opening is much stenosed and the mucous surface may be smooth or irregular with depressed and ulcerated areas. Microscopically there will be seen large amounts of dense connective tissue with a few atypical epithelial cells. Is less actively metastatic than the other forms.

In these cases the stomach may be much enlarged.

Medullary carcinoma generally appears at the pylorus, but sometimes on the wall in the lesser curvature. The growth is irregularly elevated, spongy, and cauliflower-like. Is soft and vascular and ulcerated, particularly in the center, thus forming a crater-like excavation where perforation may occur. Microscopically the epithelium predominates and retains to some extent the normal arrangement, although the individual cells rapidly become more globular and less columnar. Is actively metastatic.

Malignant adenoma or *adenocarcinoma* begins as a proliferation of the glandular tubules. The cells retain to a great

extent their usual shape and regular arrangement. Further away from the original focus the glandular conformation becomes less and less marked, until it may completely disappear and be replaced by the usual carcinomatous picture.

Colloid cancer may be localized or, what is more common, diffuse. The mucosa and submucosa may be markedly infiltrated and the surface covered by a gelatinous material. This is better seen deeper in the tissues, as that exposed is dissolved by the gastric juices. On section a yellowish

FIG. 150.—SCIRRHUS OF THE PYLORUS, CAUSING PYLORIC STENOSIS (Orth). *D*, Duodenum; *P*, pylorus; *K*, carcinomatous projections on the mucosa.

gelatinous material escapes. The cells are cylindric and there is a myxomatous degeneration of them and of the intercellular elements.

Squamous epithelioma occurs at the cardiac end of the stomach as an extension from a growth primary within the esophagus. Is very rare.

Results of Cancer of the Stomach.—The involvement generally takes place within the gastric tubules. This is soon followed by an infiltration of the submucosa, the muscularis, and finally the serous covering, upon which there appear nodules. Perforation of the wall may then occur with sub-

sequent involvement of the peritoneum; this is especially so in colloid cancer. Neighboring organs, as the liver, pancreas, and colon, may be affected by contiguity. If adhesions have formed perforation may be prevented and the neighboring tissues protected. Fistulous tracts may be opened between the stomach and duodenum or transverse colon, or with the pleura. Metastases may take place first in the neighboring lymphatics and then in more distant tissue, or secondary nodules may follow the entrance of tumor cells into veins. These are commonly carried to the liver, where they lodge and grow. The metastatic growths may be so large as to conceal the primary neoplasm. If at the pylorus there will be all the symptoms of obstruction, such as retention of food with decomposition.

Lactic acid fermentation is particularly common, as there is generally a lack of hydrochloric acid secretion. The stomach may become enormously dilated.

Following the ulcerative processes there may be extensive hemorrhage from the opening of a blood-vessel or there may be merely an oozing with the presence of the "coffee grounds" vomit.

Foreign bodies of many kinds may be found, either accidentally or intentionally swallowed. Intestinal parasites may also be present.

DISEASES OF THE INTESTINES

Malformations.—Complete absence may occur, but incomplete development is more common. There may be stenosis anywhere. The rectum may end in a blind sac, atresia ani, either low down or up in the sigmoid flexure. *Cloaca* formation refers to a condition in which there may be one common cavity acting as an outlet for the rectum and genito-urinary tracts. *Diverticula*, localized dilatations, are quite frequent, particularly *Meckel's diverticulum*. This is found in the ileum about three feet above the ileocecal valve. It is a finger-like projection of the same histologic formation as the intestine; is the remains of the omphalo-mesenteric duct. It may be adherent at the umbilicus, re-

main open, and allow feces to escape. Acquired diverticula may be present as small projections from the exterior of the gut, usually near the mesenteric attachment. They consist of mucous membrane and serosa, the muscular coat being absent. Occasionally inflammation, diverticulitis, with abscess formation, perforation and peritonitis may follow. Adhesions, also, may form with adjacent structures. *Enterocysts* are dilatations of the omphalo-mesenteric duct. There may be a *transposition* of the intestines, the colon ascending on the left and descending on the right. There is frequently an *abnormal* course of the large intestine, particularly of the transverse colon. This, instead of going directly across the upper part of the abdomen, takes a V-shaped course, the apex of the curve frequently extending as low as the pubes.

Hernia of the intestines refers to the abnormal entrance into or the passage through an opening.

Herniæ may be due to a weakening of the abdominal walls or to the failure of a canal to close. The mesentery may be longer than usual and allow very free motion, or there may be an abnormal amount of fat, causing an increase of weight. The exciting cause in most cases is sudden exertion, or it may be the result of repeated strains.

Herniæ may be *external* or *internal*, *congenital* or *acquired*.

External are those in which the hernial sac lies outside of the abdomen. *Internal* are those in which the sac lies within one of the cavities within the body.

External	Inguinal.
	Femoral.
	Umbilical.
	Obturator.
	Ischiatic.
	Labial.
	Perineal.

Internal	Winslowian.
	Mesenteric.
	Omental.
	Diaphragmatic.
	Retroperitoneal.

The sac may contain only a portion of the small intestine or there may be some of the large abdominal organs present. There is generally a constriction (neck) at the point where the

sac passes from the peritoneal cavity; below is a dilated pouch. The inner wall of the sac is composed of the peritoneum.

A hernia is *reducible* if it can be pushed back through the opening from which it escaped. If it cannot be returned it is an *irreducible* hernia. The reduction may be prevented by adhesions having formed at the neck of the sac, by the accumulation of fecal matter, by edema or other causes. There may be such a constriction at the neck as to interfere with the circulation, a *strangulated* hernia. This may result from the same conditions, in a more severe degree, as cause an irreducible hernia, or from the entrance of more viscera into the sac. It is followed by an extreme passive congestion, inflammation of neighboring tissues, and hemorrhage and gangrene. If the strangulation is relieved early before degenerative changes have set in, the intestine may resume its usual condition.

In old hernias a chronic inflammatory process may have gone on, with the formation of fibrous adhesions between the sac and neighboring coils of intestine. This is due to the circulatory disturbances resulting from the twisting or stretching of the vessels.

Obstruction of the intestine may be due to the presence of foreign bodies within its lumen, to fibrous adhesions and bands, to a twisting or volvulus, to intussusception or invagination, or as a result from the formation of cicatrices at the seat of ulcerations. It may be complete or incomplete, acute or chronic. If the obstruction has been a chronic one, there will probably be some *dilatation* of the intestine above the constricted area. In time there may be hypertrophy of the walls with inflammation and ulceration. The part below may become atrophic.

Volvulus is the twisting of the intestine resulting in obstruction. It may twist in its long axis, but usually a loop of intestine twists around its mesenteric attachment. It occurs where the mesentery is unusually long and lax. The most common seat is in the sigmoid flexure. In volvulus there is a consequent obstruction to the blood-supply, and if the condition is not rapidly remedied, thrombosis, edema, and gangrene ensue. Above the twist the intestine will be dilated,

there will be passive congestion, and frequently ulceration with perforation. Sometimes adhesions may form with a neighboring loop of intestine and no peritonitis result.

Intussusception or invagination is a condition in which one part of the intestine slips into the lumen of an adjoining part, like a glove-finger. The outer covering is called the *intussuscipiens* or sheath; the inner portion, the *intussusceptum*. Is most frequent in young babies and most common near the ileocecal valve. It may be due to convulsive or to reverse peristalsis. In children there may be found at the post-mortem table numerous invaginations which probably occurred during the death agony and have no significance.

The ensheathed portion may be very short or it may extend many feet. As a result of the invagination peristalsis is increased and the tendency is for the intussusception to become greater and greater. As the intestine is invaginated the mesentery is taken with it and the circulation is interfered with. That is followed by congestion, edema, and inflammation; a result of which is the formation of adhesions rendering the displacement permanent. If the process has been more acute, obstruction with gangrene and peritonitis usually follows. Sometimes the invaginated portion may slough off, be passed through the rectum, and the edges of the intestine unite without any peritonitis resulting. There may be merely a stenosis through which fluid contents can pass.

Occasionally the rectum may extrude from the anus—*prolapse*. It usually occurs as a result of strained defecation. Is generally very easily reduced, but is likely to recur, as the sphincter muscle is usually weak. If allowed to remain, the prolapsed portion becomes inflamed, the mucous surface ulcerated, and necrosis may occur, as a result of acute strangulation by constriction of the sphincter.

Stenosis or narrowing of the lumen sometimes occurs, usually as a result of the contraction of cicatrices formed after ulceration. The primary ulcer may be syphilitic, tuberculous, or rarely typhoidal.

The *syphilitic* ulcer has its long diameter at right angles to the long axis of the intestine, usually in the rectum just above

the sphincter, and is generally completely annular. It is characterized by extensive fibrous tissue formation, which, subsequently contracting, causes stenosis. The *tuberculous* form lies transverse to the intestine, but does not completely encircle the gut. Constriction may occur as a result. The *typhoid* ulcer has its long axis parallel to that of the intestine and does not tend to form much fibrous tissue. If there is a cicatrix formed, it usually causes a slight puckering of the intestine, very seldom resulting in stenosis.

Stenosis may result from the presence of a neoplasm within the intestine or from pressure from without.

Dilatation results from incomplete obstruction. Is most marked in the large intestine as a result of retained fecal matter which undergoes decomposition and assists in the dilatation. This condition is usually associated with localized pouches or diverticula. Are most common in the rectum.

Perforation may be due to traumatism or may result from ulceration. If the opening is a small one, it may be filled up by a plug of fibrin and no damage result; if larger, there will be an escape of fecal contents into the peritoneum, with fatal results. If the process of ulceration has been a very slow one, as in tuberculosis, such dense adhesions may have formed as to prevent the escape of fecal contents into the abdominal cavity. Instead of opening within the body the perforation may open out onto the skin surface, giving rise to a fecal fistula.

Rupture may follow injuries of the abdomen or may result from accumulations of gas.

Circulatory Disorders.—*Acute congestion* may result from active irritation or as the early stage of inflammation.

Passive congestion is common in diseases of the liver associated with engorgement of the portal veins, and to a less degree in chronic heart and lung disturbances. Local congestion is the result of some limited involvement of the mesenteric veins. The veins are swollen and prominent, the mucosa is swollen, edematous, dark bluish in color, and small petechial hemorrhages may be present.

Minute hemorrhages may occur in chronic passive con-

gestion and in hemorrhagic diatheses. Severe hemorrhage may follow ulcerations of all kinds, particularly from the typhoidal, or wounds, such as the bites of intestinal parasites.

Edema is present in chronic passive congestion, and in inflammations, particularly if severe.

Embolism and **thrombosis** may occur. As a rule, there are no bad results, as the anastomoses are so extensive that necrosis does not occur. It may, however, if the mesenteric vessels be involved, be followed by *hemorrhagic infarction* with fatal necrosis of the portion of the intestine involved and peritonitis. The formation of the duodenal ulcer in burns is thought by some to be due to thrombosis.

Amyloid degeneration beginning in the fibrous wall of the small blood-vessels of the mucosa and submucosa is quite frequently encountered in chronic tuberculosis, syphilis, and chronic suppuration.

Pigmentary infiltration is often met in old people. The muscularis is filled with a yellow pigment that does not contain iron. The intestine may become very dark as a result of the use of bismuth paste in surgery.

Hemorrhoids are varicose veins of the rectum. They may be either internal or external in character, according to their relation to the sphincter ani. Are commonly the result of interference with the venous circulation. They may be due to cirrhosis of liver, pressure from tumors, or from chronic constipation. The feces not only press upon the veins, but also give rise to a chronic proctitis that weakens the vessel walls. The hemorrhoids appear as small, dark bluish projections which on section are found to be formed of dilated veins, between which is usually a formation of fibrous tissue. The cavity may occasionally become filled with fibrin and be converted into a fibrous mass. Hemorrhage frequently accompanies hemorrhoids, and infection with inflammation is also common.

Inflammation of the intestine may affect either the small or the large intestine or any portion of them. Different names being given according to the region affected, enteritis (small intestine), colitis (large), etc. The mucosa and the submucosa

are generally involved. If there is involvement of the stomach as well, the condition is known as *gastro-enteritis*.

The inflammation may be caused by the presence of irritating substances within the gut, as indigestible materials or poisons of various kinds. It may also be due to the presence of certain organic bodies resulting from imperfect digestion and fermentation.

Among the commonest causes of enteritis are bacteria, such as the typhoid, cholera, and colon organisms. The intestinal parasites, particularly the Entamœba histolytica, can occasion extensive inflammation.

Catarrhal enteritis may occur in any portion of the small intestine. There is usually a slight congestion with some swelling. The lymphoid follicles are enlarged, there is considerable mucous exudation, and occasionally small ulcerations. There is increased peristalsis on account of the inflammation and the intestinal contents are fluid, as a result of the exudation, and frequently blood stained. Shreds of epithelium may be discharged. In the intestinal wall there is a round-cell infiltration of the mucosa, the lymphoid tissue is increased, and there is an abnormal number of goblet cells.

Follicular enteritis is frequently a sequel to the catarrhal form. In it there is marked involvement of the solitary lymphoid follicles. They are much swollen, project from the mucous membrane, and sometimes undergo suppuration with the formation of ulcers. Is probably due to infection.

Suppurative enteritis is characterized by the exudation of pus cells, with round-cell infiltration and focal abscesses in the mucosa and submucosa. May follow a follicular enteritis and show numerous ulcerations of the follicles.

Ulcerative enteritis may be due to suppuration of the lymphoid follicles in catarrhal or follicular enteritis or to specific infection, as in typhoid, dysentery, tuberculosis, and syphilis.

Pseudomembranous enteritis is characterized by the formation of a thick, grayish, soft and pulpy covering to the mucosa. Is most common in the large intestine on the edge of the valvulæ conniventes. When the membrane sloughs off, there is left exposed an ulcer. The intestinal wall is thick-

ened by edema, hyperemia, and round-cell infiltration. This form is generally seen in dysentery.

Chronic enteritis may follow the acute form or it may depend upon the persistence of the cause of irritation. It generally involves the small intestine and upper part of the large. The mucosa is thickened, even to the extent of polypoid formations, the lymph-follicles enlarged, and extensive connective-tissue hyperplasia is present. Ulcerations and stellate cicatrices of healed ulcers may be found, particularly in the large intestine. In between the elevated areas of mucosa there are depressed bands of fibrous tissue. The surface of the intestine is covered by a tenacious mucus and the color of the tissue may be very dark on account of the venous congestion. Round-cell infiltration is marked. Instead of hypertrophy there may be an atrophy of the glandular tissue, on account of the contraction of the fibrous tissue. These areas will be marked by the presence of dark almost black pigment. There is generally an atrophy of the muscularis as well.

Clinical Manifestations.—All forms of enteritis are generally accompanied by diarrhea as a consequence of the increased secretions and peristalsis. There is interference with digestion and nutrition and the general health of the individual suffers. Poisonous substances may form within the intestine.

Duodenitis generally occurs in association with gastritis. On account of the resulting edema, the common bile duct, which empties into this part of the intestine, becomes obstructed and also inflamed. This gives rise to jaundice, a common symptom of duodenitis.

Typhlitis, inflammation of the cecum, is generally due to the retention of large masses of feces, although in many instances it accompanies an appendicitis. Inflammation may involve the surrounding tissues, *perityphlitis*.

Appendicitis, inflammation of the appendix, is quite common. The lumen of the appendix being so small, it is easily obstructed by foreign bodies or by edema. The blood-supply is poor, so nutrition is readily affected. Foreign bodies,

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as inspissated feces or seeds, may set up an irritation, but inflammation is more commonly the result of the entrance of micro-organisms. Those most commonly found are streptococci, staphylococci and the colon bacillus. Anërobic forms, also, probably play an important part. Their entrance may be facilitated by lesions of the mucosa caused by foreign bodies. The organisms pass through the mucous membrane, penetrate the lymphoid tissue, and set up an acute inflammation with round-cell infiltration. *Catarrhal* appendicitis is characterized by slight swelling and minute erosions of the mucosa. The muscular and serous coats will show slight infiltration and the lumen will contain epithelial and pus cells. In the more severe form the appendix is much increased in size as a result of a thickening of the walls, not of a dilatation of the lumen. The walls are hyperemic, infiltrated with pus and fibrin, and the peritoneal coat is covered with fibrin. In the *necrotic* or *gangrenous* variety the inflammatory processes are destructive. The mucosa is

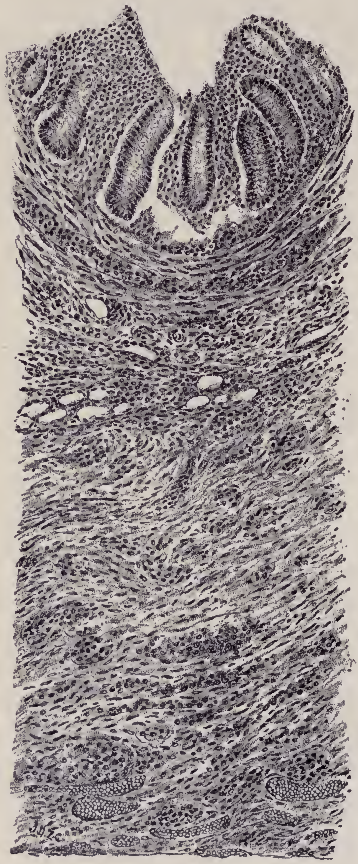

Fig. 151.—Acute Appendicitis with Round-cell Infiltration and Hyperplasia of Connective Tissue in all of the Coats (Stengel).

In large part the round cells of the mucosa and submucosa belong to the normal lymphoid tissue of these parts.

destroyed and the muscular and serous layers are soon attacked. The inflammation involves neighboring surfaces and a fibrinous peritonitis develops. This may be local, and by giving rise to adhesions between adjacent tissues no further extension takes place. The process may be very rapid and perforation follow before any restricting adhesions form; this is accompanied by a general and frequently fatal peritonitis.

In *interstitial* appendicitis there is a tendency toward excessive connective-tissue formation which generally terminates as a chronic thickening.

Appendicitis may recover spontaneously with nothing more than a slight thickening of the walls or obliteration of the lumen. Adhesions may form, and by interfering with the surrounding organs give rise to various disturbances. The appendix may rupture with local or general peritonitis or there may form a localized abscess.

Colitis, inflammation of the colon, may be restricted to some one part of the colon, as the cecum, sigmoid flexure, etc., or involve all portions. It is generally due to the retention of large masses of hard feces, or to bacterial infections; as tuberculosis and syphilis. Certain poisons, particularly the metallic, can set up severe inflammations; can also be due to products elaborated within the body, as in chronic nephritis. The mucosa is much thickened and there is a marked secretion of mucus which is mixed with exfoliated epithelium, leukocytes and red cells. The mucosa frequently ulcerates and may become covered by a pseudo-membranous substance made up of desquamated epithelium and mucus. The walls of the intestine are frequently infiltrated with pus cells and fibrin. This pseudo-membrane may be passed from the rectum, in pieces or as a cast (*mucous colitis*).

Proctitis, or inflammation of the rectum, may be due to the presence of masses of hard feces, of foreign bodies, or to infections, as tuberculosis, syphilis, and gonorrhea. If acute in onset, it however soon becomes chronic.

The mucous membrane is swollen, edematous, and minute hemorrhages are frequent. Ulcerations of varying degrees of severity are present and may give rise to a *periproctitis* and

perirectal abscesses. These may rupture externally and leave a fistulous tract opening both internally and externally; is known as *fistula in ano*.

INFECTIOUS DISEASES

Dysentery indicates an inflammatory condition of the colon and rectum characterized by ulcerations of the mucosa and the passage of numerous small, mucous, and bloody stools. It is a term that is applied to disturbances brought about by several causes. It is most common in tropic and semi-tropic, but occurs in the temperate zones as well.

It may be due to the presence of the Entamœba histolytica, to the Shiga bacillus, or to various ferments and toxins of decomposing meat; sometimes it may follow the ingestion of poisons, particularly mercury.

In the mild or *catarrhal* forms there is congestion and edema of the mucosa with some petechiæ. There is a slight increase in the secretion, and ulcerations may be found involving the solitary follicles.

The *ulcerative* or *amebic* variety is much more severe. There is at first a marked nodular swelling of the mucosa. The organisms pass between the epithelial cells of the mucosa, undermine the membrane, and by increasing in numbers separate it from the blood-supply. The mucous membrane at these points becomes necrotic and is cast off, exposing the infiltrated submucosa, which eventually sloughs off. The resulting ulcers vary greatly in size and shape, but are all characterized by having a decidedly undermined edge. Several ulcers may have communications beneath the mucosa and the ulcerations may extend to the serous covering. The amebæ will be found in the lesions. The process tends to become chronic, and for a long time the amebæ may be found in the stools, which also contain large amounts of pus.

As the inflammation subsides the ulcerations begin to cicatrize and recovery takes place. There is usually quite extensive atrophy of the mucosa and sometimes distortions due to contraction of the healed ulcers. At times a chronic thickening of the intestinal walls may follow.

The most common complication is abscess of the liver, due to the passage of micro-organisms through the veins, lymph channels, peritoneum or gall ducts from the intestinal ulcers. In amebic dysentery there is usually a single abscess. Perforation may occur; also thromboses of the veins of the colon and mesentery and of the portal vein.

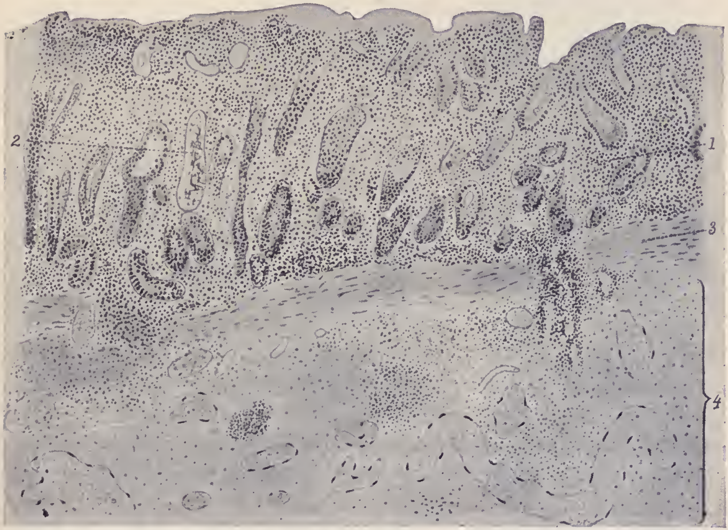

FIG. 152.—DYSENTERY OF LARGE INTESTINE. × 50 (Dürck).
The superficial layers of the mucosa are necrotic. In the deeper layers between the glands many leukocytes have accumulated (1); 2, fibrinous thrombus in a small artery; 3, muscularis mucosæ ruptured in many places by leukocytic accumulations; 4, submucosa with greatly dilated blood-vessels.

There may secondarily result a *diphtheritic* dysentery; a variety in which there is formed a pseudo-membrane which occurs in varying extent. There may be numerous small areas so covered, or the entire colon and rectum may be involved. If the process is mild, the mucous membrane is alone affected; but if severe, the submucosa may be destroyed.

In the *bacillary* form the mucous membrane is swollen,

congested, and hemorrhagic, with the surface covered by blood-stained mucus. The lymphatic tissue of the colon becomes swollen, the solitary follicles undergoing necrosis with superficial ulceration. The mucosa rapidly regenerates, with a practically complete recovery to normal.

Asiatic cholera is an acute specific inflammation of the small intestine due to the comma bacillus or vibrio.

The post-mortem appearances differ according to the time at which death occurred. Early in the disease, in the algid form, the intestine is rose-red or purple in color, the mucosa shows numerous petechial hemorrhages, and its surface is covered by a transparent layer of sticky fibrin. The contents of the intestine are thin, watery, and cloudy, and very copious. In it are many small flakes of desquamated epithelium which give rise to the "rice-water" appearance that is characteristic of the condition. The discharges are alkaline, have but little odor, and although some blood may be present, bile is seldom found. In this early stage the solitary and agminated lymph-follicles are enlarged and frequently undergo ulceration. There is no leukocytic infiltration of the deep tissues and usually very little of the mucosa. The large intestine is generally hyperemic, but otherwise negative.

In later cases, after the algid stage has disappeared, the intestine is no longer reddish in color, but is nearly empty, except for the presence of a foul-smelling gas. At this period an enteritis with the formation of a pseudo-membrane frequently occurs. This is a result of the coagulation necrosis of the mucous membrane, particularly of the tips of the villi.

The Peyer's patches are pigmented and bile may be found in the intestinal contents. The lesions are most marked in the lower portion of the small intestine, in which respect cholera differs from dysentery and poisoning by the metallic salts, which involve the large intestine.

In some cases there may be a hemorrhagic gastritis or an ulcerative colitis.

In a person dying from cholera there will be hyperemia of the pia, hyperemia and parenchymatous degeneration of

the kidney, and bronchopneumonia. The liver and spleen will be smaller than usual.

Early in the course of the disease the bacillus is present in the intestinal contents in great number, in a pure culture.

Typhoid fever is an acute infectious fever caused by the B. typhosus, and its characteristic lesion is ulceration of the lymphoid tissue of the small intestine, particularly the Peyer's patches. The upper part of the colon is also generally involved.

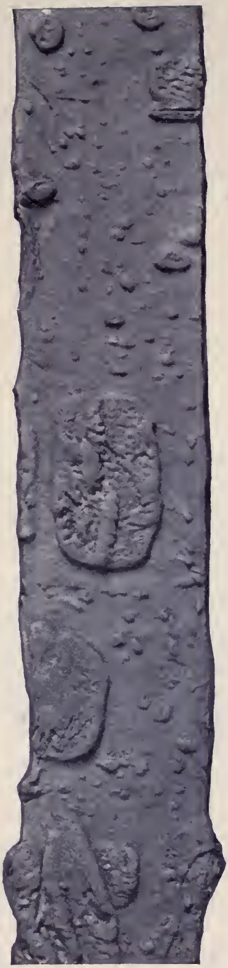

FIG. 153.—ILEUM; TYPHOID FEVER (EARLY STAGE) (Nicholls).

Peyer's patches and solitary follicles greatly swollen; superficial ulceration.

The lesions in the intestine correspond closely to the clinical course of the disease and indicate by their appearance the duration of the infection. The organisms gain entrance into the individual through the mouth in food, or more commonly in the water. They pass to the small intestine and there give rise to the various lesions. At first the mucous membrane becomes hyperemic and swollen, the solitary follicles and the Peyer's patches become larger, through hyperplasia of the lymphoid tissue, their surfaces irregular and hyperemic. In the course of a few days they fade and become quite pale or grayish-white as necrosis begins. The Peyer's patch is elevated and sharply defined from the neighboring mucosa. Microscopically the intestinal wall presents a high-grade round-cell infiltration and an increase in epithe-

lioid cells. During the second week there is a necrosis of the hyperplastic lymphoid nodes. The tissue is cast off in shreds. The greater part of the follicle may be sloughed off, leaving a long, irregular ulcer with a smooth floor lying parallel to the long axis of the intestine. The ulcers usually appear toward the end of the second week of the disease. They extend to

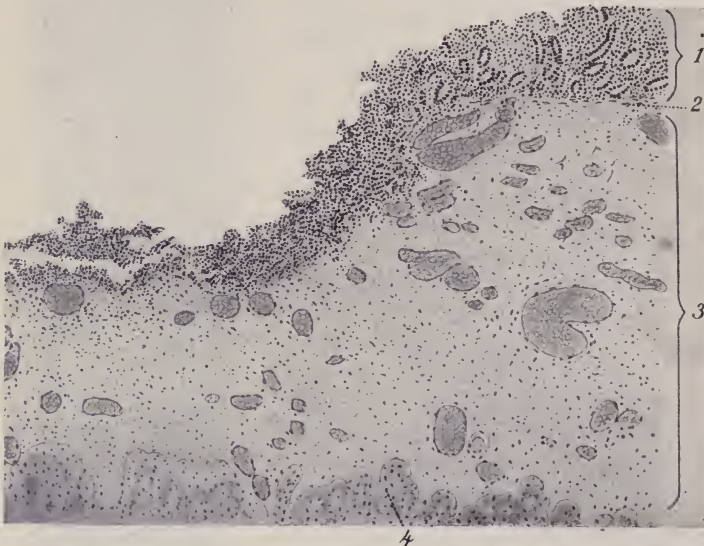

FIG. 154.—TYPHOID ULCER AFTER DETACHMENT OF SLOUGH. × 50 (Dürck).

The margins of the defect end abruptly; in the floor of the ulcer, which reaches into the submucosa, are seen a few necrotic portions of tissue with extensive infiltration of leukocytes. 1, Mucosa; 2, muscularis mucosæ; 3, submucosa with overfilled blood-vessels; 4, muscularis.

varying depths, in some cases involving the lymphoid tissue alone, but at times the necrosis passes on to the submucosa and even to the serous covering. The ulcers rarely extend beyond the limit of the lymphoid tissue. Perforation is common. Ulceration is most marked in the small intestine near the ileocecal valve.

By the end of the third week the necrosis and ulceration

cease and reparative processes begin. The hyperplastic lymphoid tissue resumes its normal condition by disintegration and absorption of the newly formed cells. The ulcerated surfaces heal by granulation and cicatrization and by extensions from the surrounding mucous membrane.

The increase in the cellular elements in the lymph-nodes is the result of the proliferation of the endothelial cells of the lymphatic spaces, blood-capillaries, and reticulum of the lymphoid tissue, and a hyperplasia of the lymphoid cells. It is brought about by the action of a mild toxin. These cells give rise to necrosis in the lymph-nodes, liver, and spleen by thrombosis which interferes with the blood-supply. They may be found in the lung.

The *complications* of typhoid fever are several, but the most serious are *hemorrhage* and *perforation*. Small hemorrhages may be the result of oozing from the ulcerated surfaces. Its presence causes the stools to be dark brown in color. Severe hemorrhage follows the destruction of the walls of some larger vessel. The blood may remain in the intestine long enough to undergo changes and give rise to the "tarry stools." Occasionally the loss may be so sudden and large that the blood is discharged when still bright in color. Perforation follows extensive ulceration, and may occur by the end of the second week, but usually later during the third. It is more probably due to necrosis of the serosa than to an increase in internal pressure. The intestinal wall, however, may have become so thin that solid substances may lacerate it and escape into the peritoneal cavity. If the process has been comparatively slow, adhesions may have formed, so as to prevent a general infection. If this has not happened, general purulent peritonitis, nearly always fatal, will be set up.

The mesenteric lymph-nodes become enlarged, soft, and hyperemic, and show a cellular proliferation similar to that in the intestinal lymphoid tissue. As the processes within the intestine increase in severity these nodes show fatty metamorphosis, softening, and even necrosis. If the patient recovers connective tissue replaces the necrotic portions. The spleen becomes much larger, soft and flabby, and hy-

peremic. Sometimes it will be the seat of infarctions and abscesses. The muscles, particularly the recti, show Zenker's degeneration, a hyaline change. Minute hemorrhages may also be present in the muscles. The heart muscle undergoes a certain amount of cloudy swelling and at times is the seat of acute myocarditis. Acute endocarditis occasionally occurs, but is not as common as in other infectious diseases. There is no leukocytosis present unless pneumonic inflammations have arisen; acute bronchopneumonia and croupous pneumonia are quite common complications. The liver, in addition to parenchymatous changes, may show minute areas of focal necrosis. The kidneys are quite commonly the seat of acute parenchymatous nephritis and areas of necrosis are also frequently observed. Hemorrhagic areas may be found.

The bacilli are present not only in the intestine but elsewhere. Early in the disease they can be readily obtained from the blood. They are found in the skin lesions, the "rose spots," also in the urine. The internal structures, as the spleen, mesenteric nodes, and gall-bladder, contain them. The organisms may remain within the body for a long time after convalescence and then give rise to suppuration, as ostitis, parotitis, and meningitis. They may be present in the gall-bladder for years and be discharged continually in the feces. Such persons are called "typhoid carriers" and may accidentally infect many others.

Pulmonary tuberculosis is a not uncommon condition occurring after the patient has apparently entirely recovered.

An important test in the making of the diagnosis of typhoid fever is the *Widal reaction.* It is based upon the principle that when the blood of a patient suffering from typhoid fever is added to a fresh culture of the typhoid organism the bacilli will gather into clusters and gradually lose their motility, a process known as "clumping." The reaction is performed as follows: The most satisfactory way is to obtain the blood in a fresh state, and if one can get a sufficient amount to allow the use of the serum alone, it is even better. A drop of blood or serum is forced out of a capillary tube, in which it should be received, and to this nine drops of sterile water are added.

This is thoroughly mixed, and one drop of this mixture added to one of the culture gives a dilution of 1 : 20. The culture to be used that is generally recommended is a bouillon one not more than twenty-four hours old. Some authors recommend a fresh agar culture, but there is danger of the bacilli being already clumped to some degree. Dilutions of 1 : 10 and 1 : 50 should also be employed as control tests. A drop of this solution is placed on a cover-glass, which is then inverted over a hollow-ground slide. The reaction is said to be positive if within forty-five minutes the bacilli are found to be gathered in little groups and their motility almost or entirely absent.

FIG. 155.—TUBERCULOUS ULCERATION OF THE INTESTINE (Stengel).

If the blood cannot be sent fluid, several drops of blood should be placed on a sterile slide, and when dry, sent to the laboratory. One of the drops is dissolved in a drop of sterile water and then diluted until the proportion is one to fifty. The rest of the technic is the same as with the fluid blood.

This reaction does not, as a rule, appear until seven to eight days after the onset of the disease, and may be delayed until much later. It may also appear in those who have suffered from typhoid fever some time previously.

Paratyphoid fever presents lesions that differ somewhat from typhoid. There are not the characteristic intestinal changes. The clinical appearance may be similar, but there may be no ulcerations present in the intestine or else the ulcers may be very irregular and not typical. Two strains of organisms very closely related to each other, but differing in certain respects in their cultural characteristics from the typhoid bacillus, have been isolated.

Tuberculosis of the intestine may occur in children as a primary infection; in adults it is frequently secondary to pulmonary and laryngeal tuberculosis. In children the source of infection is probably tuberculous milk. The consensus of opinion at present is that the tubercle bacillus found in the milk of diseased cows can infect the human organism, but does not frequently do so. The infection in adults is generally due to the swallowing of sputum.

The lymphoid tissue in the lower portion of the ileum, just above the ileocecal valve, is the usual seat of the primary lesion. There is the formation of a tubercle with coagulation necrosis; the central portion is cast off and an ulcer with thickened edges and a yellowish base is formed. Several ulcers become confluent and a large irregular one results. Instead of remaining the shape of the Peyer's patch, the ulcer tends to increase in size laterally, unlike the typhoid lesion. This is due to the extension by means of the lymphatics which surround the intestines. The lesion usually involves the submucosa as well as the mucosa, also the muscularis and sometimes the serous coat. As a rule, the peritoneal covering at the site of the ulcer is the seat of numerous small tubercles in clusters. There may also be found white lines connecting neighboring tubercles; these are probably lymph-vessels that are stopped up by caseous matter.

A peculiar hyperplastic form, involving chiefly the ileocecal region, is characterized by extensive round-cell infiltration and the formation of a large amount of connective tissue. Tubercle formation, caseous degeneration and ulceration are usually very slight. On account of the thickening of the wall

the lumen is much narrowed and at times almost completely stenosed.

Perforation is the most dangerous complication, but it does not frequently occur, on account of adhesions that have been formed during the progress of the disease. Tuberculous peritonitis may result from tuberculosis of the intestine. The ulcers may be present in all stages, some completely healed while others are undergoing active changes. As a result of the position of the ulcer the cicatrization is more likely to be followed by stenosis than is the case in typhoid fever. Stenosis, however, may occur when the tendency to organization exceeds the tendency to destruction of tissue. The mesenteric nodes are usually involved and at times may show much more marked disease than is seen within the intestine.

Syphilis of the intestine is seldom met with, and when seen usually appears in the rectum. The small intestine may be involved in cases of congenital syphilis. Small gummata are seen which show a marked tendency to undergo softening and ulceration, the lymphoid tissue being generally the site of the lesions. The rectal form is usually the result of direct infection and the disease may appear as the primary chancre, as papules and mucous patches in the secondary stage, and as gummata in the tertiary. In the third stage there may be such extensive ulceration as to destroy the mucous membrane almost completely for several inches along the bowel; the ulcer usually being at right angles to the long axis of the bowel. The wall of the intestine at the seat of ulceration may become much thickened by a round-cell infiltration. Following this extensive ulceration, cicatrization with contraction and stenosis may occur.

Actinomycosis and **leprosy** very rarely appear. **Anthrax** sometimes involves the small intestine. It occurs in woolsorters, brush-makers, and others exposed to infection. The mucosa and submucosa show hyperemia and a hemorrhagic edema, and extensive ulceration appears. The tissues are dark colored and necrotic and the ulcers are surrounded by a zone of hemorrhagic infiltration. The adjacent lymph-

nodes and the spleen are enlarged; and the anthrax bacillus can be found in greatest numbers in the locality of the necrosis.

Enteromycosis refers to a condition in which there is an infection of the intestine by the eating of decayed proteid substances, as putrid meat, fish, sausages, and so on. Sometimes occurs in epidemics. The intestinal lesions vary from a mild catarrhal enteritis to a pseudo-membranous inflammation and ulceration. Is accompanied by diarrhea and depression. The symptoms, both constitutional and local, probably depend upon the action of toxins elaborated in the decaying matter rather than upon the bacteria themselves.

Tumors.—*Connective-tissue* growths are unusual and generally benign. Fibroma, lipoma, and myxoma are sometimes seen. They may cause some obstruction if large. *Sarcoma* is rare. It arises within the submucosa and extends very rapidly, elevating the mucosa. Is generally round-cell in character and may with difficulty be distinguished from the lymphatic enlargements, lymphoma, that are present in the intestine in leukemia and Hodgkin's disease.

Epithelial tumors are more common and not infrequently cause death. *Adenomata* are quite common, and may be diffuse or of a polypoid nature. They originate from the crypts of Lieberkühn, as a rule. The polypoid form is more common in the rectum and may undergo inflammatory changes as a result of injury by the feces.

Carcinoma is the most common of the intestinal tumors and is usually composed of cylindric cells. It is most frequent at certain sites, as the papilla of the common bile-duct, the ileocecal valve, the hepatic, splenic, or sigmoid flexures, and within the rectum. It is somewhat elevated, its surface rough, irregular, and ulcerated, and it involves the entire lumen of the gut, causing obstruction. Bleeding from the ulcerated surface is quite common. If the connective-tissue stroma predominates the growth is hard and firm; if very cellular, it is soft, whitish, and spongy. These tumors show a marked tendency to undergo mucoid and colloid degenerations, and metastases to the neighboring lymph-nodes, peritoneum and liver are common.

Squamous epithelioma originate at the anus and may involve neighboring structures.

Parasites of both animal and vegetable types are common occupants of the intestine. Of the *animal parasites*, the round worms, as the Ascaris lumbricoides, Oxyuris vermicularis, Trichiuris trichiura, Anguillula intestinalis and stercoralis, and Eustrongylus gigas; the tape-worms, Tænia solium, T. saginata, T. echinococcus, and Dibothriocephalus latus; and the sucking worms, the Ankylostoma, are found present under various circumstances.

Other and more unusual forms are the Cercomonas, Trichomonas, Balantidium coli, and the Entamœba coli and hystolytica.

Foreign bodies of innumerable varieties have been swallowed and subsequently found within the intestine. Sometimes dense masses of fecal concretions, enteroliths, are found. These are composed of a nucleus of epithelium, hair, or other foreign bodies, surrounded by dried fecal matter. They may give rise to local irritation. In the lower animals they are of large size, but in man are generally small.

Tympanites or *meteorism* is a condition of dilatation of the intestine by the presence of a large amount of gas. It may be so severe as to cause a paralysis of the muscular coat with a cessation of peristalsis.

DISEASES OF THE LIVER

Malformations are not common and seldom of importance. Complete absence is seen in acardiac monsters. Variations in the number of lobes and in the fissures may occur. Portions of hepatic tissue may be separated from the main mass, but are usually connected by a pedicle of connective tissue. Malformations may be acquired particularly as a result of tight lacing, which causes a deep transverse notch upon the anterior surface which may almost divide the organ, the hepatic tissue along the line of pressure undergoing atrophy.

The position of the liver may be changed by relaxation of its ligaments or by pressure from tumors within the abdomen.

The ribs posteriorly and the right crus of the diaphragm may by pressure form long furrows.

Disturbances of Circulation.—The liver is peculiar in its blood-supply in that it contains two systems. One of these, the lesser, supplies nutrition to the stroma; the other, which is of much greater importance, supplies the blood necessary for the carrying on of the hepatic functions. This latter, the portal system, divides into many branches that ramify throughout the acini and empty into the central veins of the lobules, branches of the hepatic. The blood flows very slowly through the organ and is under very little pressure, consequently is readily interfered with by slight obstruction.

Anemia may be part of a general anemia or may be due to pressure upon the blood-vessels. The organ is pale, but may vary in color according to the amount of bile or of fatty degeneration present.

Active hyperemia occurs normally during digestion, and is also present as an accompaniment of inflammation, in which case the areas are circumscribed. May be general as a part of an infectious process. The organ is slightly enlarged, softer, dark red in color, and on section blood readily escapes.

Passive hyperemia is of greater pathologic importance than the active. It is caused by interference with the escape of the blood into the vena cava. Is found in valvular diseases of the heart, in those conditions interfering with the pulmonary circulation, as emphysema, chronic fibroid phthisis, etc., and may be due to pressure upon the vena cava by tumors. Pleural effusions with adhesions may cause it.

As a result of the obstruction to the circulation the central vein of the lobule first becomes dilated, and subsequently the capillaries in communication. Following this continued pressure there is atrophy of the cells in the central zone and at times even of those as far out as the periphery of the lobule.

The organ is at first enlarged, the anterior edge rounded, and may be darker in color. On section is seen the characteristic reddish-brown and yellow mottling known as the "nutmeg liver." The congestion of the central vein and

its adjacent capillaries produces a reddish-brown central zone in the lobule. Next comes a zone in which atrophic pigmented liver-cells remaining between the dilated capillaries cause a brownish color. Still further toward the periphery of the lobules is a pale yellow zone of liver-cells

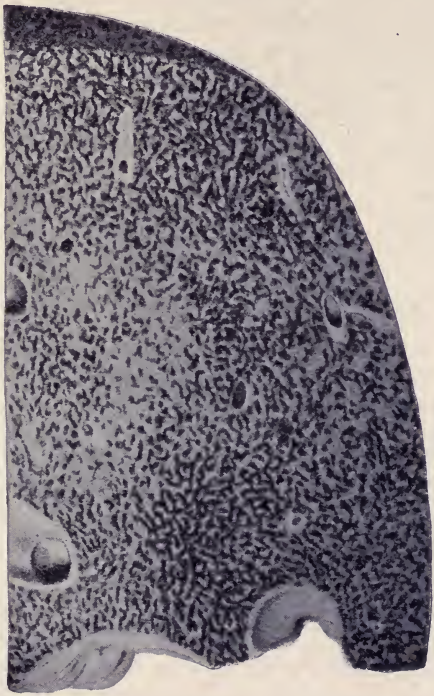

FIG. 156.—NUTMEG LIVER: CHRONIC CONGESTION DUE TO CARDIAC DISEASE (Bollinger).

that have undergone fatty degeneration. This area will frequently show some bile stasis.

"The microscopic examination shows that in the early stages the intralobular venules and capillaries are dilated and overfilled with blood, the dilatation extending a variable distance toward the periphery of the lobules, depending upon

the degree and duration of the process. The blood content of the capillaries consists not infrequently of a disproportionate number of leukocytes, which may be interpreted as evidence of stasis. More or less extensive hemorrhage into the centers of the lobules and consequent destruction of the hepatic parenchyma is not uncommon. It is found especially in cases of acute heart failure and in cases of chronic failure of compensation terminating in a sudden and complete breakdown. The hepatic cells about the central vein show a varying degree of atrophy—partially a pressure atrophy, and partly doubtless nutritional, the result of insufficient oxidation. In most cases there is a considerable accumulation of fat in the liver cells; in some cases this is excessive and accounts for the term "fatty nutmeg" liver. Usually the cells about the central venules contain more or less pigment derived from hemoglobin, usually in the form of hematoidin, but hemosiderin, as well, may be present."

If the congestion has been present for a long time the organ may become smaller, on account of atrophy of the hepatic cells, and firmer. The surface of the liver becomes uneven, due to hyperplasia of connective tissue, and is darkly pigmented, a condition known as *cyanotic induration*.

In some cases there is a deposit of hematogenous pigment throughout the organ, causing it to be dark red. Such a change is spoken of as *red atrophy*, as the liver is smaller than normal.

As a result of chronic congestion the action of the liver may be much interfered with, one of the most common symptoms being slight jaundice, probably due to the obstruction of the bile-ducts and capillaries by the swollen endothelial cells. The bile is also generally more viscid than normal.

Embolism and *thrombosis* not infrequently occur and cause greater or less disturbances according to their location and magnitude. As a rule, no serious conditions arise, as the collateral circulation is so extensive. The hepatic artery is capable of supplying sufficient blood for both the nutrition and function of the organ, so that marked interference with the portal circulation does not necessarily result in infarctions.

If the portal vein is completely obstructed, the secretion of bile stops, the blood is retained in the portal system, and death may result. If the hepatic artery is obstructed the liver rapidly becomes necrotic.

Numerous small foci of necrosis may result from infectious emboli in the portal capillaries. Is known as *focal necrosis* and is seen in puerperal fever, and in septic conditions involving the portal system, also in various infectious diseases. These foci differ in color from red to yellow according to whether blood or fat is present in the greater amount. The interlobular portal vessels are frequently the seat of a hyaline thrombosis.

Infarctions of the liver, either hemorrhagic or anemic, are almost unknown, as the anastomoses of the hepatic vessels are so extensive.

Hemorrhage of the liver occurs in severe infections and intoxications.

INFILTRATION AND DEGENERATION

Pigmentation of the liver may be *hematogenous.* The blood coloring-matter may not be completely transformed into bile-pigment and is deposited in the interlobular tissues, in the peripheral zones, and in the central area of the lobule. This occurs to some degree in nearly all diseases of the liver. Is marked in chronic congestion, amyloid disease, cirrhosis, and pernicious anemia. The pigment is found as dark brown granules, is probably hemosiderin, as it gives the iron reaction, a blue color when pure sulphuric acid and potassium ferrocyanid are added.

Biliary pigment due to the retention of bile is not uncommon. The liver becomes dark yellowish-green, at times almost black in color. Is most marked in the central zone of the liver lobules.

Pigment in the form of melanin resulting from blood destruction in chronic malaria, and also as anthracotic particles, is found occasionally.

Fatty infiltration is to a certain extent normal, is more marked the younger the individual. After a meal, parti-

cularly if rich in fat, there is an infiltration in the peripheral zones. This is soon removed if the hepatic functions are being carried on normally. If the oxidation does not take place properly the fatty infiltration may become of an extremely high grade. Is best seen in chronic tuberculosis, particularly if forced feeding has been indulged in, in marasmatic individuals and in alcoholics, especially when malt liquors have been consumed to excess.

The liver becomes much enlarged, is at times nearly twice its normal size; the edges are rounded, its color is a uniform yellow, and it is doughy, slight pressure causing an indentation. On section the knife will be covered with small droplets of fat. The center of the acini may be darker than the periphery on account of congestion. The cells, microscopically, are seen to contain comparatively large droplets of fats which show a marked tendency to coalesce and form one large drop which may greatly distend the cell and push aside its nucleus, giving rise to the "signet-ring" appearance. The infiltration begins in the periphery and extends inward. On account of the distention of the cells the blood-vessels may be hidden from view and so obstructed as to give rise to considerable anemia and diminishment of functional activity.

The cells in this condition do not appear to be much damaged and are apparently able to resume their work when the fat disappears.

Parenchymatous degeneration or cloudy swelling occurs in most of the infectious fevers and in intoxications. The liver is somewhat enlarged and grayish-yellow in color. Microscopically the cells are seen to be swollen and filled with albuminous particles which obscure the nucleus. The organ readily recovers if the exciting cause passes away, otherwise fatty degeneration will ensue.

Fatty degeneration or metamorphosis occurs in severe anemias, in phosphorous and arsenic poisoning, and in certain of the infections, as yellow fever. The liver is smaller than normal, yellow in color, and soft. Oil drops exude from the cut surface. Microscopically the cells are seen to contain numerous minute fat granules that do not, as a rule,

tend to coalesce. Is most marked in *acute yellow atrophy* of the liver. In it the liver is greatly decreased in size, the edges thin, its color uniformly yellowish or streaked with brown, and is very soft, so much so that it may not retain its shape. The capsule is much wrinkled. On section the tissue in many places seems almost liquid, while elsewhere it is firmer and darker in color. Oil fairly drips from the surface. Microscopically the cells are seen to have undergone extreme metamorphosis, and to have been replaced by pigment. The hepatic tissue may be completely destroyed to a great extent; the degenerated material is absorbed and the decrease in size results.

Occasionally bright red or dark red areas are present. These represent foci of hemorrhagic infiltration or pigmentation.

The causes of this condition are practically unknown. It is most common in young women. It appears in infectious fevers, particularly puerperal, in syphilis, in phosphorous poisoning, and again without any apparent cause. Micro-organisms of many kinds have been found in the bile-vessels and in the hepatic tissue, but no specific one has been isolated. Some authors think it due to the absorption of toxins from the intestine.

The destruction apparently begins in the peripheral zone around the portal vessel and extends toward the center.

The urine contains leucin and tyrosin.

Amyloid degeneration of the liver results from long-continued suppuration, as in chronic tuberculosis, in suppurative bone diseases, and is usually accompanied by similar degeneration elsewhere. The liver is larger than normal, a little pale in color, and is quite firm. The cut surface frequently appears quite translucent and may be a grayish-white or a dull yellow color.

The degeneration begins in the wall of the intralobular capillaries, which become much thickened; so much so that the blood-supply may become obstructed. Pressure is also exerted upon the adjacent liver-cells, many of which undergo atrophy. The peripheral zone is the one in which the change is first noticed, and from there it extends toward the center of

the lobule. The connective tissue is also involved and the affected areas may become very extensive. As the epithelium is involved secondarily the organ is able to carry on its function as long as a sufficiently large number of cells do not become atrophic.

Edema of the liver occurs in the course of long-continued circulatory disturbances and in severe infections. The tissue is swollen and many of the cells may contain vacuoles.

Atrophy as a primary condition depending upon local anemia is rare. Is quite common as a secondary lesion, depending upon pressure, such as tight lacing, or that resulting from the contraction of cicatricial bands. The organ becomes irregularly atrophic, the cells in the involved areas are distorted, irregular, granular, and pigmented. The nuclei generally break down.

In *leukemia* there are collections of lymphocytes in the connective tissue between the lobules.

Acute interstitial inflammation of the liver usually follows upon acute infectious conditions elsewhere, particularly in the intestines, but may be due to trauma. Is always suppurative in character and may appear as a single large abscess or as numerous small ones. The exciting microorganism may gain a foothold in the liver by means of (1) the portal vein, (2) the hepatic artery, (3) the hepatic veins, (4) the umbilical vein in the newborn, (5) the bile-ducts.

The organisms lodging as emboli within the capillaries set up a focus of suppuration.

Infection from amebic dysentery generally gives rise to a single large abscess in the right lobe. The pus contained within such differs from that ordinarily found in that it is grayish or pinkish in color, and mucilaginous in consistency. The exciting organism may be present.

In bacillary dysentery numerous miliary suppurative foci are found.

In suppurative thrombophlebitis (pylephlebitis) the purulent process follows along the course of the infected vessels, where it can be seen in the form of soft, white lines of suppuration with inflammatory reaction in the adjoining tissue.

The liver-cells degenerate, lose their nuclei, and become necrotic. At the same time there is extensive round-cell infiltration within as well as around the lobules. Pus cells soon appear and a small focus of suppuration is formed. This process may continue until a large abscess results.

If the abscesses are small the organ may regain an approximately normal condition through absorption of the pus with

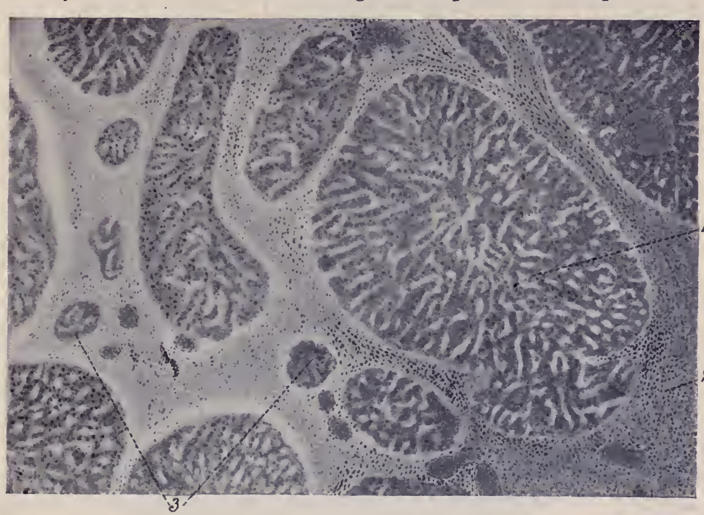

FIG. 157.—ATROPHIC CIRRHOSIS OF THE LIVER. × 40 (Dürck).

Well-marked bands of connective-tissue (2) divide the parenchyma of the liver into irregular islands of varying size; even in the larger of these there is no division into lobules (1). Vena centralis absent in some places; in others, excentric (upper right corner). 3. Smaller islands of liver cells. Scattered heaps of round cells in the connective tissue and toward the left a few epithelial canals with darkly colored nuclei (newly formed bile-ducts).

cicatrization. Large abscesses may very slowly become absorbed and their walls much thickened; lime salts may be deposited.

Instead of a favorable termination the abscess may rupture into the abdomen, into the thorax, or if adhesions have formed through the abdominal wall.

Chronic interstitial hepatitis is characterized by an overgrowth of fibrous connective tissue supposed to be due to the long-continued action of some mild irritant. Alcohol is thought to be the commonest cause.

The more usual form is that resulting from the irritating substance being conveyed in the blood, *hematogenous;* a second and rare form is the *hepatogenous*, one in which the changes follow upon an obstruction to the bile-vessels.

Portal or Atrophic Cirrhosis (*Laennec's Cirrhosis, "Hobnail" Liver*).—Is hematogenous in character, as in the majority of cases it is due to the presence, in the circulation, of a poisonous substance formed by distilled liquors. Early in the disease the organ may be somewhat enlarged, but in the typical stage the liver is small, contracted, the surface irregular, the color varying greatly, is very hard, dense, and cuts with great difficulty. The nodules that project are composed of liver-cells, while the depressed areas are formed by bands of connective tissue that have contracted. These bands are grayish in color, the elevated portions yellowish or brownish, the color depending upon the fatty degeneration or the presence of bile. As a rule such a liver will weigh more than usual on account of the increase in the density of the tissue.

Microscopically the process begins as a localized infiltration of round cells about the interlobular branches of the portal vein. This is followed by a proliferation of the connective tissue with the formation of new fibers. These increase in number, and undergoing contraction interfere with the portal circulation. The blood-vessels will show endarteritis or thrombosis. This gives rise to certain associated symptoms, as ascites 4 to 15 liters of clear fluid may be present, gastro-intestinal catarrh, hemorrhoids, and distention of the superficial abdominal veins (the caput medusæ). Jaundice is seldom present. Hemorrhage, with hematemesis, due to rupture of various veins of the esophagus or of the cardiac end of the stomach may occur. There may also be an oozing from the gastric mucosa. The entire lobule eventually becomes surrounded, and as the contraction continues the

hepatic cells undergo atrophy till at last there may be an island composed of a few epithelial elements. The connective tissue does not tend to become intralobular.

Associated with the above changes is more or less marked fatty degeneration. An important feature in this disease is the proliferation of bile-ducts in the interlobular connective tissue. There is usually a decided increase in their number

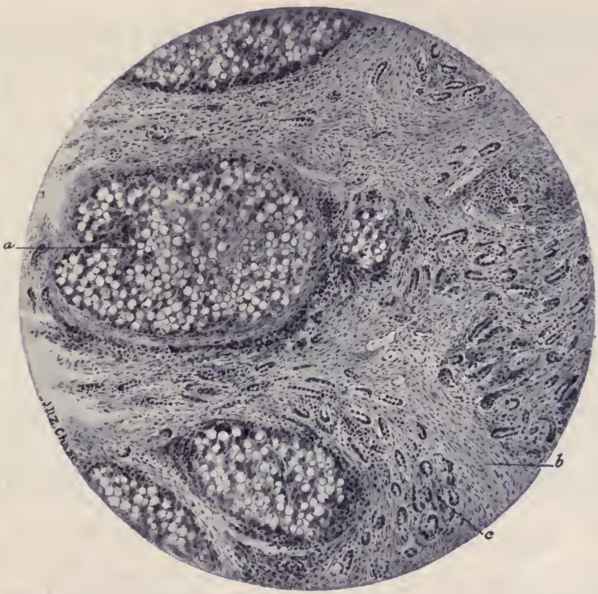

FIG. 158.—CHRONIC INDURATING CIRRHOSIS OF THE LIVER (McFarland). *a*, Liver lobule, most of whose cells are in a fatty infiltrated condition; *b*, greatly hypertrophied periportal connective tissue; *c*, proliferated bile-ducts.

derived from pre-existing ducts or from a reversion of the liver cells to the less specialized type.

Sometimes the liver-cells may contain large amounts of pigment granules, varying in shade from yellow to dark green; may be hemosiderin or bile-pigment.

Biliary or Hypertrophic Cirrhosis (*Hanot's Cirrhosis*).—In this form the liver is larger than normal, 2000 to 4000

grams, and the main lesion is an inflammation of the minute bile capillaries between the columns of liver-cells. Is probably of an infectious origin.

Its surface is smooth or finely granular, dense and firm, and cuts with difficulty, but not with so much as in the atrophic form. The cut surface shows usually a decidedly mottled appearance, areas of yellow, gray, and green being intermingled. The connective tissue is not seen in bands surrounding islands of liver-cells, but occurs in a diffuse arrangement. It does not tend to contract and interference with the portal circulation is unusual.

Microscopically the new-formed connective tissue is seen to extend into the lobules between the columns of cells as well as in the interlobular areas. Proliferation and desquamation of the epithelium of the small biliary ducts occur and lead to obstruction with subsequent dilatation. There is also a multiplication of the pre-existing ducts, with the formation of new ones through a reversion of the liver epithelium. Surrounding them is an increase of connective tissue, a periangiocholitis. The number of bile-ducts may be so great as to give rise to a condition resembling an adenoma or even a carcinoma.

On account of the obstruction to the ducts jaundice is present and the liver may be dark green in color.

Portal Cirrhosis. (Laennec's)	Biliary Cirrhosis. (Hanot's)
Acute, 3 years or less.	Chronic, 5 to 10 years.
Small. Surface uneven, pale.	Large. Surface smooth, mottled green.
Connective tissue surrounding acini.	Connective tissue generally diffused and extending into acini.
Ascites appears early and often severe.	Appears late if at all.
Jaundice rarely present.	Jaundice comes on early and is very marked.
Hemorrhoids common.	Unusual.
Hemorrhage early, often profuse hematemesis.	Hemorrhage occurs late and is slight.

Obstructive biliary cirrhosis is a condition in which there has been an overgrowth of connective tissue as a result of ob-

struction of the large bile-ducts. The congestion of the bile in itself acts as an irritant, but there is usually an infection by micro-organisms from the intestine. The liver becomes swollen, and inflammatory reactions appear. The surface is smooth and the tissue is deeply stained by the bile. The peripheral zones of the acini show small areas of necrosis which may become transformed into minute abscesses if

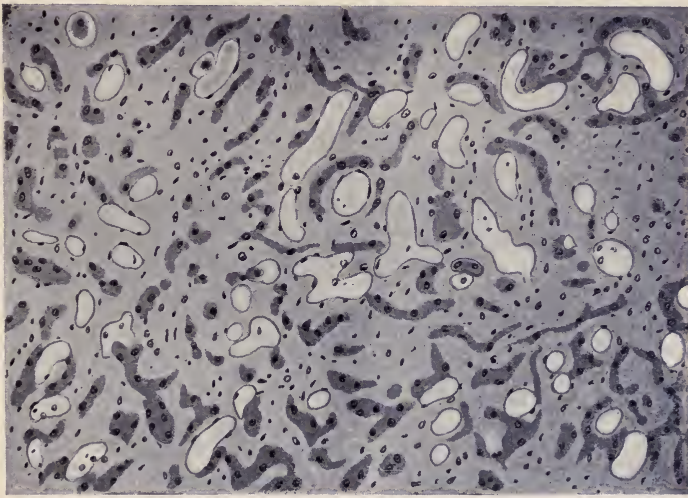

FIG. 159.—(HYPERTROPHIC) DIFFUSE CIRRHOSIS OF THE LIVER. × 160 (Dürck).

Lobular marking lost, the liver tissue separated into narrow strands by proliferating young connective tissue with short fibers, in which are wide capillaries with distinct endothelium.

bacteria are present. Instead of suppurating, the necrotic areas may be replaced by connective tissue and give rise to wide-spread induration that closely resembles hypertrophic cirrhosis.

The bile-ducts may increase in number, and evidences of regeneration of the hepatic cells are shown by the presence of mitotic figures.

This form generally follows obstruction of one of the

larger hepatic ducts or of the common duct. If the obstruction has been complete, rapid fatty degeneration and acute atrophy may occur.

Perihepatitis or inflammation of the capsule of the liver may be present in cirrhosis and as a result of chronic peritonitis. The capsule may become greatly thickened and by contraction bring about atrophy of the hepatic tissue immediately underlying.

Rupture of the liver usually results from direct injury. Is more commonly seen in the newly born when there has been instrumental interference.

INFECTIOUS DISEASES OF THE LIVER

Tuberculosis of the liver is secondary to lesions of the disease elsewhere, particularly of the peritoneum, and is probably transmitted through the blood. It appears generally as miliary tubercles scattered throughout the organ, or as larger necrotic foci. Rarely there is a single large cheesy focus.

Microscopically the lesions are the same typical ones as are found everywhere in the disease. Such a liver is usually fatty, but may show amyloid changes.

Syphilis of the liver is a common involvement in that disease. In adults who have acquired syphilis there is frequently a diffuse proliferation of connective tissue with atrophy of the hepatic cells that closely resembles atrophic cirrhosis. Generally the disease manifests itself in the form of localized proliferations of connective tissue that divide the liver into numerous small but well-defined lobes. This results from the T. pallidum getting into the circulation, becoming lodged in the minute vessels and producing a toxin that causes the hyperplasia. A certain area may become almost constricted off from the rest of the organs. The irregular distribution of the connective tissue is the characteristic feature. This form probably originates as an inflammatory thickening about the portal veins and the bile-ducts.

Gumma may also be present in acquired or congenital syphilis, either singly or in numbers. In the acquired form

the single ones are usually the larger. They occur as rounded yellowish masses, the center of the larger ones frequently being the seat of coagulation necrosis. Surrounding them is a zone of hyperemia and there is generally some connective-tissue hyperplasia. This occurs in the form of bands radiating from the center, giving a characteristic stellate appearance to the resulting scar.

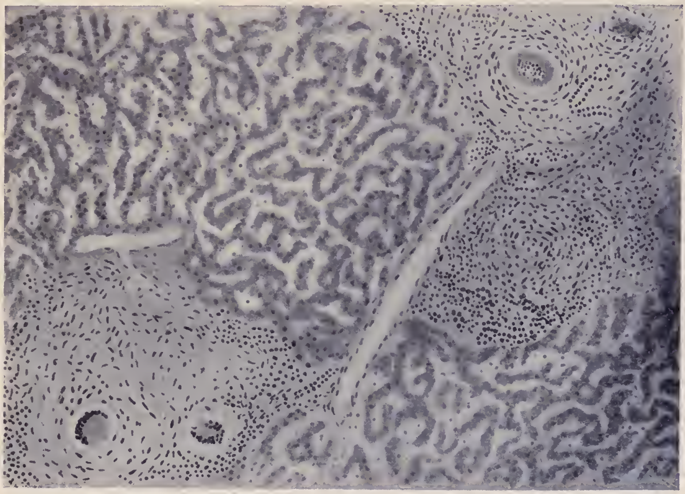

FIG. 160.—MILIARY TUBERCULOSIS OF THE LIVER. × 70 (Dürck).
Two foci, consisting of smaller confluent tubercles, which are still distinguishable. The giant cells are rounded. The foci are situated in the periportal tissue in the vicinity of a portal branch.

Congenital syphilis of the liver may manifest itself in a diffuse form or as gummata. In the diffuse variety there is a wide-spread connective-tissue proliferation, resembling that of biliary cirrhosis, and round-cell infiltration. The organ is yellowish or brown, sometimes larger than normal, and extremely firm, almost like sole leather. The round-cell infiltration is found in the neighborhood of the blood-vessels, even being seen within the walls. The liver epithelium is frequently the seat of fatty degeneration, giving

rise to the "acute yellow atrophy" of the liver of the newborn.

The congenital gummata are not, as a rule, circumscribed. They are found in the interlobular tissue and may be located within the wall of a blood-vessel or of a bile-duct.

Leprosy is sometimes found in the liver, where it occurs as granulomatous masses containing the characteristic giant cells and bacilli.

Actinomycosis rarely occurs in the liver. When present, it is generally due to secondary involvement by extension from the lung.

Tumors.—Primary growths of the liver are very unusual, but it is nearly always involved secondarily in malignant disease of other localities.

Angioma is about the most frequent new growth. It generally occurs upon the surface of the liver as small, circumscribed, dark red or purplish areas that may be single or multiple. Sometimes they may be as large as an orange. They are more common in old, poorly nourished people. The surrounding liver tissue shows no changes. Microscopically the structure is that of a cavernous angioma.

Fibroma, *Lipoma*, and *Myoma* are very rarely met with.

Sarcoma may be primary or secondary, the latter being the more usual.

The primary variety is more frequently found in children. It develops from the connective tissue of the hilus or of the periportal tissue and appears either as a round-cell or a spindle-cell growth.

Secondary sarcoma follows as a hematogenous infection from a primary focus elsewhere, and is formed of the same variety of cells as the original growth. Melanotic growths are commonly secondary to sarcoma of the eye.

The liver is increased in size and is the seat of numerous rounded masses varying in size and pale in color.

Adenoma is found in livers that are otherwise normal, and also in cases of cirrhosis. May be single or multiple, nodular, somewhat encapsulated, and grayish or pinkish in color. At times it may be difficult to distinguish adenoma and cir-

rhosis from carcinoma both by the naked eye and by the microscope.

Hypernephroma, a variety of adenoma that develops from a misplaced fragment of the cortical portion of adrenal tissue, is but rarely seen. The cells in this form are cubical and contain fat and pigments.

Carcinoma may be primary, which is uncommon, or secondary, which is the usual form.

Primary cancer may appear as a large, more or less circumscribed tumor, usually in the right lobe. It probably originates as an adenoma and extends into the surrounding tissues. Microscopically there are seen irregular cell nests surrounded by a well-marked connective-tissue framework. The cells resemble the liver parenchyma, as a rule, but in places they are smaller and more closely simulate the cells of the bile-ducts. Fatty degeneration, with necrosis and interstitial hemorrhage, is common, and pigment, either biliary or melanotic, is not infrequently present.

Another variety of the primary growth occurs as a diffuse carcinomatous infiltration with a general increase in the size of the organ. The surface of the liver is granular and nodular, and grayish or brownish in color. Larger circumscribed nodules may also be present. Except for the large nodules, the appearance of the organ is very similar to that in cirrhosis.

Microscopically it is seen that the entire tissue is infiltrated by the cancer cells. Surrounding these collections of cells are bands of connective tissue, and lying in between the two is a narrow zone composed of atrophic liver-cells that have been pushed aside by the neoplastic cells. The capillaries are found to be filled with cancer cells and the infiltration may become so great as to obliterate blood-vessels and bile-ducts and completely destroy the function of the liver.

A third variety of primary cancer is the interlobular form. In this the carcinoma has extended along the distribution of the portal vein and invades but slightly the neighboring tissue. The liver appears to the naked eye very much like an atrophic cirrhosis, having the same irregular surface. Is frequently spoken of as cirrhotic cancer.

Secondary cancer is frequently found in cases of primary growths of the stomach, intestine, pancreas, mammary glands, and uterus. Occurs in connection with those organs whose venous blood empties into the portal system. It generally appears in the form of numerous nodules disseminated through the organ. The nodes vary greatly in size, the large ones frequently showing a depressed, umbilicated center, the result of necrosis and softening with absorption. These secondary growths are, as a rule, quite well circumscribed. The cells that compose them resemble more or less closely those of the original neoplasm. Masses of these cells gain entrance into the circulation as emboli, and wherever they lodge they undergo division and give rise to new tumors.

Cysts of the liver are unusual. Are usually formed by the dilation of a bile-duct, but may be due to an obstruction of the lymphatics.

Echinococcus cysts are comparatively common. Are caused by the Tænia echinococcus, a parasite of the dog. The cysts may be either unilocular or multilocular; in the latter case they may occupy the greater part of the organ. The wall of the cyst consists of an outer connective-tissue layer and an inner cellular layer from which secondary cysts may grow.

These cysts by their pressure cause atrophy of the liver substance, icterus, and ascites. They may rupture into the abdomen, neighboring organs, or at times into the vena cava with general distribution. If bacteria gain entrance, the cysts may become transformed into an abscess. Occasionally the contents of the cysts may be absorbed and replaced by cicatricial tissue.

Parasites.—The most common and important is the larva of the Tænia echinococcus, which gives rise to the cysts above described. *Entamœba histolytica* in cases of tropical dysentery gains entrance and frequently gives rise to abscess formation, usually single. *Coccidium oviforme*, a common protozoön in lower animals, has been found in man. It forms growths that resemble somewhat adenomata. The *Fasciola hepaticum*, *Dicrocœlium lanceolatum*, in the bile-ducts, and the *Schistosomum hæmatobium*, in the portal vein, are sometimes seen.

DISEASES OF THE GALL-BLADDER AND BILE-DUCTS

Angiocholitis or **cholangitis,** inflammation of the bile-ducts, is generally found in the common duct. It may, however, extend throughout the smaller ducts and capillaries. Is commonly secondary to inflammatory conditions in the stomach or duodenum. May be due to bacteria entering from the intestine or to irritation by the presence of a gall-stone. In the *catarrhal* form the mucosa becomes reddened, swollen, edematous and covered by mucus.

In the *suppurative* type the biliary ducts are dilated, filled with purulent material, commonly stained with bile. The walls of the ducts are much thickened, softened and infiltrated by pus. The mucosa is congested, edematous, covered with mucus and in advanced cases, irregularly ulcerated. About the terminal branches of the ducts there are usually small abscesses. The liver is enlarged, swollen, softened and opaque. The surface is irregular in consequence of the projection of many small abscesses. The cut surface shows more or less enormously dilated bile-ducts filled with pus. The intervening liver tissue is the seat of marked periductal congestion, parenchymatous degeneration and necrosis.

If the swelling subsides bile begins to circulate and the symptoms cease. If there has been permanent obstruction to the duct by connective-tissue formation, secondary changes within the liver take place, such as obstructive biliary cirrhosis.

Cholecystitis is an inflammation of the gall-bladder. It is commonly due to gall-stones within, but may be due to infection from without, particularly in typhoid fever. When gall-stones are present the cystic duct is obstructed, the bile is unable to escape, and the gall-bladder becomes distended. The coloring-matter of the bile may eventually be absorbed and the bladder be filled with a colorless fluid. From the pressure of gall-stones ulcers may form and perforation into the peritoneal cavity, into the intestine, or through the abdominal wall occur.

In the *acute catarrhal* type the gall-bladder is distended and tense. The walls swollen, edematous and softened. The

mucosa congested and covered by mucous. The peritoneal covering may be involved with fibrin formation and adhesions. The cystic duct is partially obstructed.

In the *suppurative* form there is marked congestion, desquamation, with a fibrinopurulent exudate and more or less ulceration. The cyst wall is dark red, green or blackish. The ulcerations may lead to perforation, local abscess or general peritonitis. Cystic duct is occluded. Dense adhesions may form.

If the process becomes chronic the gall-bladder may become greatly dilated with a thinning of the walls. In other cases it may become very small, sclerotic, and at times obliterated.

Stenosis of the bile-ducts is generally due to obstruction in acute inflammation by the thickening of the mucous membrane and the presence of mucus. In chronic inflammation there may be an overgrowth of connective tissue. Foreign bodies within or neoplasm from without may press upon the ducts and obstruct them. According to the location of the stenosis different conditions result. If the cystic duct be closed, the liver tissue is unaffected, but the bile is unable to escape from the gall-bladder, which becomes much distended. If the hepatic duct is obstructed, all the smaller ducts and capillaries above become dilated by the retained bile, and infection frequently occurs, giving rise to a suppurative cholangitis. Obstruction of the common duct will give rise to the dilatation of both gall-bladder and biliary ducts. As a result the liver becomes enlarged and deeply stained by bile-pigments. The cells in the outer zone of the acini contain pigment granules, and there is frequently an overgrowth of fibrous tissue along the ducts. Areas of necrosis may also be present.

Cholelithiasis.—Gall-stones, calculi of the gall-bladder, are solid masses resulting from the precipitation of various substances from the bile. They are most frequently found late in life and most commonly in women. It would seem that they form about a nucleus composed of desquamated epithelium, bacteria, the typhoid and colon especially, thickened mucus, or a foreign body from outside. Upon this body is deposited a layer of biliary salts; more layers are built up until

a fairly large stone is found. This process is hastened if there is stasis, some decomposition of the bile, and a low-grade catarrhal inflammation. Instead of one large stone, several may form, or there may be thousands, like grains of sand.

The shape depends upon the number present. If single, it may be round or ovoid. Usually the sides are flattened by mutual pressure, giving an irregular crystal-like form. The color of the stones varies, according to their composition,

Fig. 161.—Types of Gall-stones. (From a photograph in the collection of Dr. Jepson, Sioux City, Ia.)

a, Caused complete intestinal obstruction for eight days; *b* and *c* were removed from the gall-bladder and show points of attrition; *d*, solitary stone removed from gall-bladder; no point of attrition; *e*, gall-stone of irregular shape, due to compression or moulding; *f*, solitary stone from common duct.

from light yellow, through various shades of brown to black.

They are generally formed in the gall-bladder, but may originate in the larger ducts.

The common variety is yellowish or brownish and is composed mainly of cholesterin and bilirubin in combination.

Other forms of calculi are made up of cholesterin, of bilirubin, and of calcium carbonate.

Although biliary calculi may exist for years without giving rise to any disturbances, they frequently cause more or less serious lesions. The gall-bladder generally shows some catarrhal inflammation, accompanied by some obstruction to

the free flow of bile. The walls may exhibit slight or marked changes, they may be much thickened, ulcerated, or pouched. The mucosa must not be entirely destroyed or the cholesterin-producing function will be lost. The calculi may escape from the gall-bladder as a result of ulceration with perforation. Is fairly common in cholelithiasis and most frequently perforate externally.

The most severe symptoms result when one of the calculi escapes from the gall-bladder into the cystic and common bile-ducts. This gives rise to biliary colic, a very severe form of pain which is associated with symptoms of collapse. If the stone is small, it can pass on through the ducts into the intestine. It may, however, become lodged in the lower part of the common duct, usually just above the outlet into the duodenal papilla. Following the blocking of the common duct there is retention of bile, which if long-continued gives rise to marked jaundice and lesions within the liver. The flow of bile may be resumed by dislodgment of the stone or by the establishment of a passage around the foreign body.

An accompanying symptom of biliary colic is an intermittent fever in which the temperature may go up to 104° or 105° F. at the onset. It then subsides and reoccurs.

Tumors of the gall-bladder are quite uncommon. About the only form is a primary carcinoma arising from the mucous glands. This growth seems to be quite frequently associated with gall-stones, which may be causative or merely the results of the stagnation of the bile. The liver is soon secondarily involved by direct extension.

Jaundice or icterus is a staining of the tissues by biliary pigments that have been conveyed by the blood-stream. It is a symptom common to most diseases of the liver. There were formerly thought to be two forms of jaundice, the obstructive or hepatogenous and the non-obstructive or hematogenous. The latter variety probably does not really exist, all icterus being due to biliary coloring-matter. There are, however, cases in which no mechanical obstruction can be observed, either by absence of bile in the feces or by lesions in the liver. This discoloration is seen in some infectious

diseases and after experiments in which various substances have been injected into the blood. By the destruction of red cells, hemoglobin is set free and this material, from which the bile pigments are formed, is provided in excess.

Catarrhal jaundice resulting from obstruction to the duct by an inflammation of its mucous membrane is the commonest form. Any obstruction from within or without, will, however, cause it. Microscopically it is seen that the biliary capillaries are distended and the liver cells contain more or less pigment. The bile escapes from its normal channels, is taken up by the lymphatics, from which it passes into the circulation and thence to the tissues throughout the body. The secretions and exudations of the body may be distinctly tinged. The tissue first stained is the intima of the blood-vessels; finally the skin and the sclera, where it is seen most characteristically. According to the duration, the color will vary from a light yellow to a dark bronze-green; the longer continued, the darker the color. If little or no bile escapes, the feces will usually be very light in color, clay-like.

The retention of bile within the body is generally accompanied by quite marked disturbances, particularly of the nervous system. As the flow of bile is re-established the discoloration gradually disappears.

PANCREAS

Malformations are unusual, except that the pancreas may frequently be composed of separated segments. Fragments of pancreatic tissue are sometimes found in the omentum, the walls of the intestine or of the stomach. Variations of the ducts are very common. The duct of Wirsung may be double, its relation to the duct of Santorini may vary greatly. Both ducts may open separately into the duodenum. Usually the duct of Wirsung and the common bile-duct open into the diverticulum of Vater.

Active hyperemia is present during digestion and as a stage in inflammation. *Passive hyperemia* occurs when there is some obstruction to the portal circulation. Is common in alcoholics and may lead to the formation of connective tissue.

Acute hemorrhagic pancreatitis is an uncommon condition of unsettled origin. It occurs in men rather than in women and seems to be associated in many cases with cholelithiasis. By obstruction of the diverticulum of Vater bile

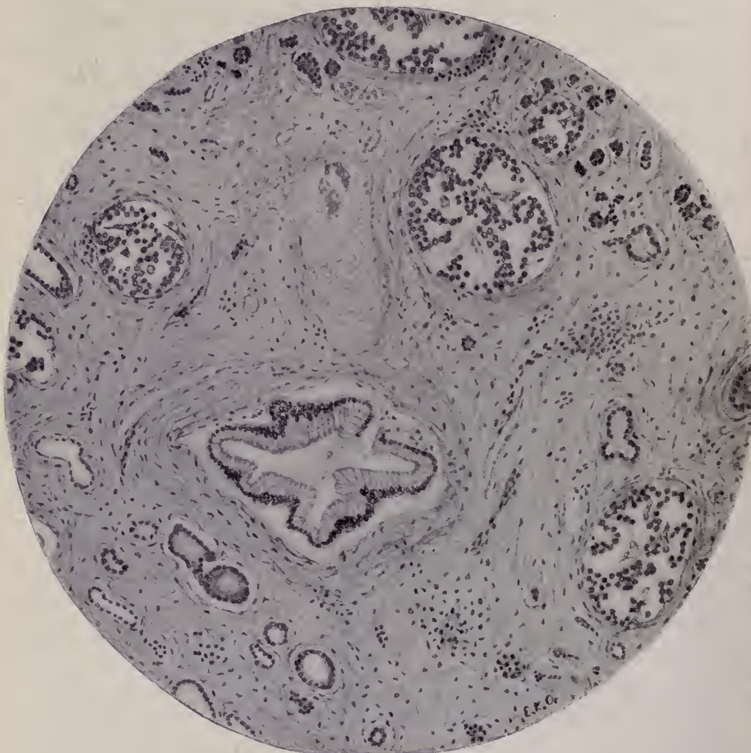

Fig. 162.—Chronic Interstitial Pancreatitis Following Duct Obstruction, showing Islands of Langerhans unchanged though Embedded in Sclerotic Tissue (Opie).

may be forced up into the duct of the pancreas and give rise to hemorrhagic pancreatitis. Various irritating substances when injected into the duct of Wirsung have given rise to a similar condition. The greater part of the pan-

creas is generally involved and death frequently comes on quite suddenly. Microscopically there is found extensive necrosis of the parenchyma and of the interstitial tissue as well. The stroma is the seat of a marked round-cell infiltration and the fat frequently contains areas of necrosis. The epithelium is the seat of fatty degeneration and may be no longer recognizable.

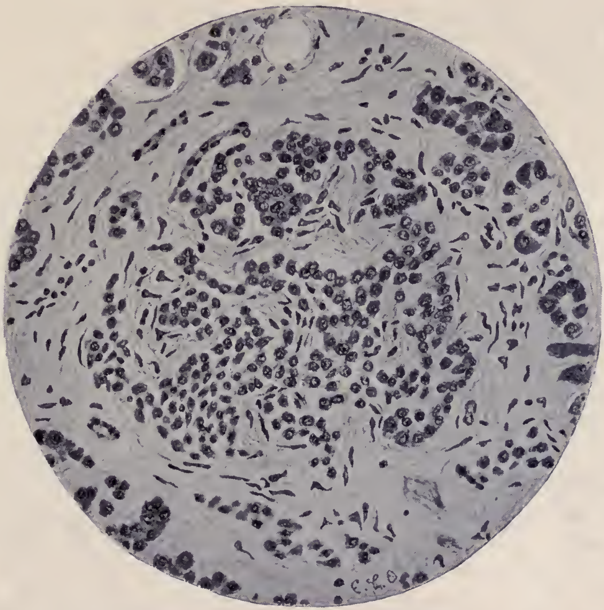

FIG. 163.—CHRONIC INTERSTITIAL PANCREATITIS OF INTRA-ACINAR TYPE, SHOWING THE INVASION OF AN ISLAND OF LANGERHANS BY THE INFLAMMATORY PROCESS (Opie).

Blood-vessels may be eroded and hemorrhage occur. Is impossible to sharply separate pancreatic hemorrhage from hemorrhagic pancreatitis.

Purulent pancreatitis may originate as such primarily or it may follow the hemorrhagic form. There may be a diffuse leukocytic infiltration or a formation of miliary foci of sup-

puration with here and there distinct abscesses. The infection may be due to the extension of inflammatory processes of a neighboring organ.

Gangrenous pancreatitis in many cases is a sequel of the acute hemorrhagic or it may follow the purulent variety. The gland is swollen, dark red, and soft; and may be converted into a dark, slate-colored, bad smelling mass. The entire gland may at last be changed into a large necrotic mass. Accompanying these changes numerous scattered foci of fat necrosis occur.

Chronic or interstitial pancreatitis is characterized by an overgrowth of fibrous tissue with more or less atrophy of the parenchyma. The connective tissue may be increased, either interlobular or intra-acinar. In the interlobular variety the islands of Langerhans are unchanged, while in the intra-acinar form the fibrous tissue surrounds and invades them. It is at times associated with cirrhosis of the liver.

Syphilitic pancreatitis is not unusual in congenital cases. There is diffuse proliferation of fibrous tissue between the lobules and the acini. The cells also atrophy and disappear and the blood-vessels are the seat of a periarteritis. The islands of Langerhans are not affected. Gumma is rare, a few cases only having been reported.

Tuberculosis is infrequently met with, but may occur in the miliary form or, what is more rare, as a large caseous mass.

Atrophy of the pancreas is frequently found in old age, in local disturbances of the circulation, cachexia, diabetes, and emaciation.

Hanseman's form of atrophy is consequent upon chronic inflammation. The organ is diminished in size and flattened, the fibrous tissue is usually adherent to adjacent organs, the epithelial elements are atrophic and are in part replaced by connective tissue. Hanseman thought that this form of atrophy was always present in cases of diabetes. Opie has found, however, that it is only in the intra-acinar form in which there is a hyaline degeneration of the islands of Langerhans that diabetes occurs.

Fatty infiltration is not infrequently found accompany-

ing various of the infectious fevers. The fat is deposited chiefly in the interlobular connective tissue and causes a secondary atrophy of the parenchymatous cells which may also contain some fat. The organ may be a trifle enlarged, soft, and grayish in color.

Fatty metamorphosis occurs as a result of severe infection, as in chronic phosphorous poisoning. The organ is soft and cloudy white.

Fat necrosis is a peculiar form of degeneration taking place in the fatty tissues of the pancreas and omentum. It appears as small, opaque, sharply circumscribed, white areas in the immediate neighborhood of the pancreas or scattered throughout the organ itself. Several areas may become confluent and involve a large portion of the pancreas. The necrotic areas may be more widely disseminated, involving the omentum and the subperitoneal and the retroperitoneal tissue. They are opaque, whitish or yellowish, are sharply defined from the normal fat, and are generally surrounded by a narrow hemorrhagic zone. Their size varies from a pin's head to that of a pea, sometimes larger.

Microscopically the affected tissues show absence of nuclei with presence of fat crystals and lime salts.

This form of necrosis is due to obstruction of the outflow of the secretion, or to the escape of the pancreatic juice into the peritoneal cavity. A fat-splitting ferment is present and it breaks up the fat into glycerin and a fatty acid. The acids are deposited as needle-like crystals with the broken-down cell. The glycerin is absorbed and the acids unite with calcium to form calcium salts, which give a gritty feel when the tissue is cut.

In the majority of cases fat necrosis is associated with either hemorrhagic or gangrenous pancreatitis.

Amyloid degeneration is found in cases of general amyloid disease, occurring either in spots or in streaks.

Hyaline degeneration is met with quite frequently. It involves the islands of Langerhans as well as the parenchymatous tissue. The affected portions stain with eosin and picric acid, but do not give the amyloid reaction.

This lesion is thought to have a distinct relation to diabetes mellitus. The islands of Langerhans are most numerous in the tail of the pancreas. In certain cases of diabetes there has been a marked absence of these bodies, due to hyaline change. The parenchymatous cells in such cases may or may not be involved. It would appear that as long as the islands remain unaffected diabetes will not be present, no matter how seriously involved the parenchyma is. These peculiar bodies of Langerhans apparently exert a distinct influence upon the metabolism of sugar.

As diabetes can be caused by lesions of the fourth ventricle it is evident that all cases cannot depend upon pancreatic lesions, but there is a distinct association in many cases.

Pigmentation may be due to hemorrhage, to atrophy, or old age. The epithelial cells contain brownish or yellowish granules that do not give an iron reaction.

Hemochromatosis is a form of chronic intra-acinar pancreatitis plus the deposit of an iron-containing pigment in the liver, pancreas, other glands, and the skin. Is accompanied by a degeneration of the parenchymatous cells and a chronic interstitial inflammation of the organs. May be present in bronzed diabetes.

Tumors.—*Sarcoma* is rare, but the round-cell and angiomatous forms have been described. They may occur as a part of a secondary sarcomatosis.

Carcinoma may occur primarily or after a similar growth in the stomach, duodenum, or gall-bladder. The primary form is found in the head of the gland and is most commonly scirrhus. It soon spreads and forms a large mass involving the greater part of the pancreas and the adjacent tissues. As it grows it may obstruct the bile-ducts, giving rise to an icterus that gradually increases in severity, or by pressure upon the duct of Wirsung set up a chronic interstitial pancreatitis sometimes accompanied by diabetes.

The growths generally originate from the cells of the acini and give an adenomatous structure to the tissue. They may arise from the cylindric epithelium of the ducts and form a scirrhous mass.

Obstruction of the pancreatic duct may cause it to become greatly dilated, so much so as to cause actual cyst formation. The contents are usually clear, but by infection may become purulent. Occasionally small cysts may be scattered through the organ.

Calculi in the duct are sometimes found. They may be a cause of obstruction.

Cysts occasionally occur. May be due to a retention of the secretion on account of obstruction of the ducts; such are usually small. Multilocular papillary cysts may result from a proliferation of the epithelial elements. Hemorrhagic cysts may follow severe traumatism.

The cystic contents are generally viscid, but may be clear and watery, or else contain varying amounts of blood. Ferments may be present.

DISEASES OF THE PERITONEUM

Malformations are occasionally met with. The omentum may be very small or unduly long. The mesentery may be very long, giving rise to enteroptosis. May allow hernias.

Circulatory Disturbances.—*Active hyperemia*, either localized or diffuse, is present during the early stage of inflammation, and is also met with in relation to tubercles and neoplasms. *Passive hyperemia* follows obstruction to the portal circulation. The veins may become much distended and tortuous and small hemorrhages into the subperitoneal tissue may be present.

Hemorrhage beneath the peritoneum in the form of petechiæ and irregular streaks is found in chronic passive congestion, in asphyxia, in phosphorous poisoning, and in some infections.

Hemorrhage into the peritoneal cavity results from rupture of a blood-vessel. When as a consequence of traumatism any of the internal viscera, as spleen or liver, rupture, blood will be present. Is also found in cases of rupture of abdominal aneurysms, and of extra-uterine pregnancy and, from typhoid or other perforations.

The blood collects in the dependent portion of the abdo-

men and may coagulate or remain fluid. If the patient recovers, the blood may be absorbed without any permanent changes, although adhesions sometimes form.

Ascites or a collection of serous fluid within the peritoneal cavity is frequently seen. It may be due to obstruction of the portal circulation, especially in atrophic cirrhosis of the liver or as a part of a general dropsical condition in cardiac and renal disease.

It is also found in some local diseases of the peritoneum, as tuberculosis, etc.

The ascitic fluid is generally clear, straw-colored, specific gravity 1008 to 1015, with a small amount of albumin, which rarely coagulates spontaneously. The amount may vary from a few cubic centimeters to several liters and may become so great as to cause marked inconvenience by distending the abdominal cavity and by pushing the diaphragm upward. This latter may cause extreme dyspnea. If the fluid is removed, it frequently collects again and again. If adhesions have formed, there may be localized collections of fluid.

If there has been obstruction to the thoracic duct, the ascitic fluid is frequently milky in character, due to the presence of chyle (*chylous ascites*). This fluid contains fat droplets as well as the red and white cells that are ordinarily present, and endothelial cells from the peritoneum.

Sometimes there may be a collection of fluid between the layers of the omentum.

When the ascites has existed for a long time there is nearly always a secondary chronic inflammation of the peritoneum with thickening.

Peritonitis, inflammation of the peritoneum, may be primary or secondary. This serous membrane covers such a large surface and so readily absorbs fluids that infection may take place with comparative ease.

Primary or idiopathic acute peritonitis arises through the infecting agent being carried by the blood from a pyogenic focus in some distant part of the body.

Secondary acute peritonitis is the more common form. It follows local injury to the peritoneum, as a result of injury

or disease, the infecting agent being carried generally by the lymphatics.

Peritonitis is brought about by infectious inflammations of neighboring tissues, particularly in septic conditions of the female genital organs, by perforations of the stomach or intestines, by appendicitis, by strangulation of the bowels, etc.

According to the extent of the lesion the peritonitis may be localized or general. The severity of the disease also differs greatly.

The membrane at the point of infection is at first hyperemic, is dull, and a serous or serofibrinous exudation soon appears. This rapidly becomes purulent or may have been so from the beginning. If the process has not been a very rapid one the affected area will be covered by a thick whitish or creamy layer of fibrin. As the exudate increases in quantity it collects in localized pockets among the coils of intestine. The fibrin may undergo organization, adhesions form between the loops of the intestine, the omentum, the abdominal walls, and other organs, and the purulent matter be surrounded and walled off. It may be absorbed, infiltrated with lime salts, or replaced by fibrous tissue. The pus may burrow and empty either externally or into some hollow organ. If the adhesions have not been sufficiently dense, the abscess may break through and infect the greater part of the peritoneum. In such a severe form the serous membrane becomes infiltrated and partially disorganized.

Localized peritonitis is not usually fatal, but in the general form recovery is rare. When peritonitis subsides and the individual lives, adhesions of varying extent remain. These eventually become transformed into dense fibrous bands that may cause very severe trouble by binding the coils of intestine together or by so compressing them that the bowel becomes more or less obstructed.

As a result of the acute inflammation the peristaltic action of the intestines is at first stopped by spasmodic contractions. In a very short time the muscle fibers become paralyzed and there is then almost complete cessation of motion. General septicemia may follow the peritonitis.

In the newborn, peritonitis generally follows septic infection of the umbilical cord.

Chronic peritonitis may follow in the course of acute peritonitis, particularly if it were localized or it may occur independently. When encapsulated collections of pus have failed to be absorbed the peritoneum adjacent shows marked chronic thickening. The omentum is frequently shortened and rolled up. A serous or other exudate may be present. Local thickenings may also be due to chronic disease of the underlying organ. This is particularly the case at times on the liver and spleen. The membrane becomes very thick, white and smooth, and resembles icing of a cake, the so-called "Zuckerguss" organs. Chronic peritonitis is particularly common in the neighborhood of the female genitalia; all of which, uterus, tubes, and ovaries, may be united by dense bands of connective tissue. Is also always present in tuberculosis of the peritoneum.

Tuberculosis of the peritoneum is seldom primary, but is commonly found as a secondary lesion in similar disease of the intestine, or mesenteric lymph-nodes. The condition may be local, being limited to the peritoneal surface of the intestine overlying tuberculous ulcers; or it may be widely disseminated as a general miliary involvement. The lesions may coalesce and form large caseous areas or there may be extensive connective-tissue formation with adhesions causing the intestines to be bound together in one dense mass. Occasionally there may be considerable serous exudate present; if the exudate is purulent it generally indicates that there has been a secondary infection by pus-producing organisms. The exudate may at times be completely absorbed or remain as sacculated collections. The tubercles may heal by granulation and cicatrization and the individual get well.

The mesenteric lymph-nodes are generally enlarged and caseous.

Tumors.—Primary tumors are unusual, new growths being generally metastatic or the result of direct extension. *Fibroma* and *lipoma* are sometimes seen. *Sarcoma* is rare.

Endotheliomata are quite frequently found, originating probably from the endothelium of the subperitoneal lymph channels and not from the flat cells lining the peritoneum. As a rule they do not occur as localized growths but are distributed throughout the peritoneum, giving somewhat the appearance of tuberculosis. The omentum is probably the seat of the primary growth.

Carcinoma is nearly always secondary, but it is thought that primary carcinoma might arise from fragments of epithelial tissues, from fetal remnants, or from portions of intestine pinched off in fetal life. There is usually a general distribution of tumor nodes of all sizes over the greater part of the peritoneum. When the nodules are widely distributed the condition is known as "*carcinomatosis*." There is always some inflammatory reaction, so adhesions are quite common. The carcinoma may extend from various abdominal organs, as the uterus, tubes and ovaries, and intestines. A gelatinous or colloid cancer of the stomach or intestine is usually soon followed by a similar growth involving the peritoneum. Such a tumor contains large and small masses of clear colloid material resulting from degeneration of the cells.

Cysts are sometimes encountered, the usual form being due to a dilatation of lymph-vessels.

Parasites are rare, but echinococcus cysts have been found as well as filaria and actinomyces.

CHAPTER XXII

DISEASES OF THE URINARY ORGANS

THE KIDNEYS

Malformations.—Rarely both kidneys may be absent, but the fetus is incapable of living. Absence of one kidney is more common and is not incompatible with life. The left organ is usually wanting and the right undergoes compensatory hypertrophy so as to perform its extra work.

Atrophy of a kidney is not infrequent, it being represented by a small body composed of connective tissue with very little glandular structure. A third kidney has been seen in a few cases. The *lobulation* of the kidneys during fetal life usually disappears by the tenth year, but it may persist till late life.

Horseshoe kidney is the result of the fusion of the two kidneys at either their upper or lower ends. The band of union may be purely fibrous or of renal tissue. The ureters, from two to four, arise from an anterior pelvis. The vessels are usually more numerous than normal and are generally anomalous.

One of the kidneys, usually the right, may become much displaced downward and hang from a much stretched peritoneal covering. Is the "floating kidney" and can give rise to many symptoms. The left may be displaced congenitally. The relaxation of the support of the right kidney may be due to disease or displacement of the liver, to tight lacing, or to a dragging exerted by the stomach or transverse colon. The perirenal fat decreases, the peritoneal covering stretches, and the kidney is easily moved. The nerves and vessels and the ureters are put in a state of tension and severe symptoms arise. If the pedicle becomes twisted the circula-

tion may suffer and by obstruction to the ureter urine collect and give rise to a hydronephrosis.

Circulatory Disturbances.—*Anemia* of the kidneys is present in general anemia; or it may be due to gradual obstruction of the arteries, either by disease or by pressure from without. If the obstruction has been sudden, necrosis is usually present. The organ is small and light in color. If the anemia continues, there is interference with the secretion of urine and atrophy may ensue. Fatty degeneration appears first in the glomeruli but soon involves the parenchyma.

Acute hyperemia is generally a stage of acute inflammation in infectious conditions. Numerous irritating bodies that are excreted through the kidneys may give rise to the hyperemia. Such are certain poisons, as cantharides, carbolic acid, toxins of infectious conditions, as scarlet fever, those present in cases of extensive superficial burns. The kidneys are slightly enlarged, dark red in color, and soft. The capsule strips easily and on section much blood escapes. In the cortex are seen numerous minute red spots, the Malpighian bodies, and the congestion exists throughout. The epithelium usually shows some cloudy swelling. The urine may contain a few erythrocytes, a trace of albumin, and cylindroids.

Passive hyperemia may be due to cardiac or pulmonary disease, to thrombosis of the inferior vena cava or of the renal veins, or to pressure upon these veins from without. Sometimes there may be an acute passive stasis, the organ becomes much distended and death may result. Ordinarily the kidney is enlarged, dark in color, and soft, with a capsule that strips readily. The stellate veins are prominent, blood drips from the cut surface, the Malpighian bodies are enlarged and the bases of the pyramids are markedly congested. If the hyperemia is of long standing there is always more or less hyperplasia of the connective tissue. So much so that the organ, although enlarged, may be hard and dark in color, owing to the deposition of pigment; is known as *cyanotic induration.* The capsule is usually somewhat adherent and the surface of the organ irregular. The epithelial cells show some fatty degeneration and atrophy.

The amount of urine is diminished and contains varying numbers of red and white blood-corpuscles, some albumin, and a few hyaline or granular tube casts.

Hemorrhage in the form of punctate collections may occur in severe acute or passive hyperemia. The blood will be found within the interstitial tissues, in the tubules, or in Bowman's capsule; it may escape by actual rupture or by diapedesis. Large hemorrhages usually occur only as a result of trauma, but may be due to infarction. The urine will contain blood either as free corpuscles or as the so-called blood-cast.

Arteriosclerosis.—The kidney may show most marked sclerotic changes, such as are found elsewhere in the body. All the vessels are not uniformly involved, so there are irregular appearances. The vessels become gradually occluded by a thickening of the walls with a decrease in the lumen. The areas supplied by such vessels undergo atrophy, degeneration, and frequently become infiltrated with lime salts. Fibrous connective tissue forms to some extent, and as this contracts it compresses the urinary tubules. Excretion continues, the tubules dilate, and small retention cysts form both on the surface and in the kidney tissue. The kidney is smaller than normal, red or grayish-red, firm, and its surface shows depressed areas representing the atrophic portions, at which points the capsule may strip with difficulty. The cortex is diminished in thickness.

Microscopically the alterations in the blood-vessels are seen and the glomeruli in many instances are surrounded by greatly thickened capsules which may contract until the capillary tufts have been reduced to small fibrous masses. If there is much connective tissue present it indicates that there has been a chronic inflammation of the organ, an interstitial nephritis. This is not uncommon, as the same etiologic factors will bring about both the arteriosclerotic and the interstitial changes. Is caused by syphilis, chronic lead poisoning, gout, and old age.

In this form the urine is practically unchanged.

Infarcts of the kidney are common, as the arteries have practically no anastomoses with each other. In the *anemic*

infarct the appearance varies according to the age of the lesion. When recent, there is a pale, circumscribed elevation on the surface of the kidney, surrounded by a narrow zone of hemorrhage. If old and connective-tissue formation has occurred, there is a depressed area. On section it is seen that the involved portion is conical in shape with the apex directed toward the hilum. The epithelium becomes cloudy and soon degenerates. This area becomes transformed into scar tissue in the course of time. In *hemorrhagic* infarcts the process is the same except that the area has become filled with blood which gives it its dark appearance.

Thrombosis of the larger renal veins may give rise to congestion and edema with degeneration and necrosis of the area involved.

Embolism is not uncommon, and on account of the lack of anastomoses of the renal arteries usually results in infarction. Embolism may be single or multiple, and if bacteria are present suppurative processes are present in addition to the already mentioned lesions.

Degenerations.—*Parenchymatous degeneration* or *cloudy swelling* is a condition in which the secreting epithelium is involved. It occurs in diphtheria, scarlet fever, and in most of the infectious diseases.

If the conditions that bring about this change persist, the cloudy swelling is very apt to pass over into the acute parenchymatous nephritis. In cloudy swelling the kidney is larger than normal, somewhat softer, and yellowish or pale gray. The cut surface shows the Malpighian bodies as small red dots and the pyramids are often markedly congested. The cells in the tubules are swollen and cloudy on account of the presence of numerous minute granules, and the nuclei are hidden. The kidney may return to the normal or else acute Bright's disease or fatty degeneration may ensue.

Fatty degeneration may follow cloudy swelling or arise as a consequence of various diseases, as pernicious anemia or tuberculosis. As fat is never normally present in renal epithelium, its occurrence is always pathologic and is indicative of a degenerative process. It is due to the lack of

nutrition, and at times is added a toxic effect of some substance in the circulating blood.

The kidney is about the normal size or smaller, is soft, the cortex is not thinned, and the organ is uniformly yellowish unless there is much congestion present. The fat may be diffusely present, or, what is quite common, occur in streaks along the collecting tubules of the pyramids. It is also seen

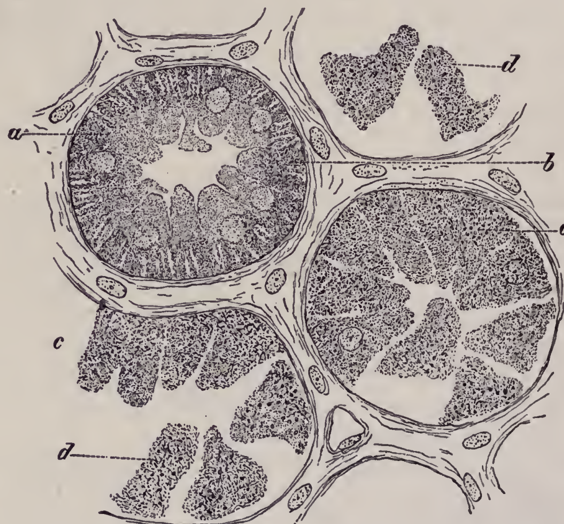

FIG. 164.—CLOUDY SWELLING OF THE KIDNEY EPITHELIUM. ×800 (Ziegler).

a, Normal epithelium; *b*, beginning cloudy swelling; *c*, marked degeneration; *d*, desquamated degenerated epithelium.

as minute yellow points. The cells contain granules or oil drops of varying size.

Amyloid degeneration of the kidney follows the same causes as bring it about in the liver and spleen, such as the long-continued suppuration in bone diseases, in tuberculosis, and in syphilis. The kidney is usually much enlarged, harder than normal, and grayish or slightly yellowish in color. If the process is not general the organ will appear mottled, areas of

fatty degeneration being present. This degeneration begins, as a rule, in the capillaries of the glomeruli, from which it extends to the neighboring connective tissue, but not to the epithelium. If the degeneration has not been extensive fatty changes are uncommon, as the blood-supply may still be sufficient for the nutrition of the epithelium. Microscopically the glomeruli are seen to consist of a homogeneous and translucent mass in which the capillaries cannot be distinguished. The capsule of Bowman may also be involved. As the circulation is interfered with the organ becomes anemic, and fatty degeneration of the epithelium occurs. The amyloid areas give a mahogany brown color on the addition of Lugol's iodin solution. The urine is diminished and contains albumin and hyaline casts occasionally.

Glycogen is found in the epithelium in the loops of Henle in cases of diabetes. The cells, instead of being granular, are homogeneous and give the dark brown color with iodin if the tissue has not been put in watery fluids. Glycogen differs from amyloid in being soluble in water.

Calcification may take place in old degenerated areas in the connective tissue or in the necrotic epithelial cells. Under this heading come the so-called "calcareous infarcts," in which various salts are deposited, particularly in the straight collecting tubules. They may be composed of urates, and the presence of such infarcts has been thought to indicate that a newborn child has breathed.

Nephritis, inflammation of the kidney, or Bright's disease is brought about by many conditions, all of which in some way produce an irritation of the kidney by means of the circulation. It follows in the course of poisoning by certain chemicals, such as arsenic, mercury, phosphorus, cantharides, and turpentine; especially in the course of the acute infectious diseases, and also in certain chronic infections, as syphilis and tuberculosis. Nephritis may be acute or chronic and *parenchymatous* or *interstitial*, according to whether the changes in the epithelium or in the connective tissue predominate. If both are more or less equally involved the term *diffuse* is applied.

Acute parenchymatous nephritis is found in the course

of the acute infectious fevers, particularly in diphtheria, scarlet fever, and smallpox, and is due to diffusible toxins. The kidneys are usually enlarged, soft, and edematous, the cortex pale and the stellate veins injected. The capsule strips easily, although tense, and the kidney may bulge through the incision. On section, bloody fluid escapes. The cortex

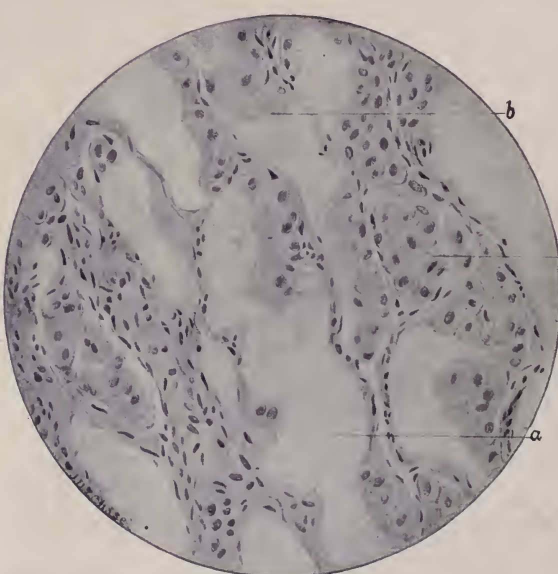

FIG. 165.—ACUTE PARENCHYMATOUS NEPHRITIS (CATARRHAL) (McFarland).

a, Tubule denuded of a large part of its epithelium; *b*, cells in a condition of degeneration; *c*, mass of desquamated cells in a tubule.

is thicker than normal and is much paler than the medulla, which is dark red. The glomeruli may appear as minute red dots. The anemia of the cortex is due to the swelling of the cells, which compress the capillaries. The epithelium is swollen, cloudy, and in many places has become desquamated. This is most marked in the convoluted tubules.

In some cases, particularly in scarlet fever, the changes

may be most noticeable in the glomeruli, the *glomerulo-nephritis*. In this variety the capsular space contains desquamated epithelium from the capsule, red and white blood-cells, granular matter, and an albuminous exudate. The cells may show fatty degeneration. The erythrocytes may be sufficiently numerous to form blood casts.

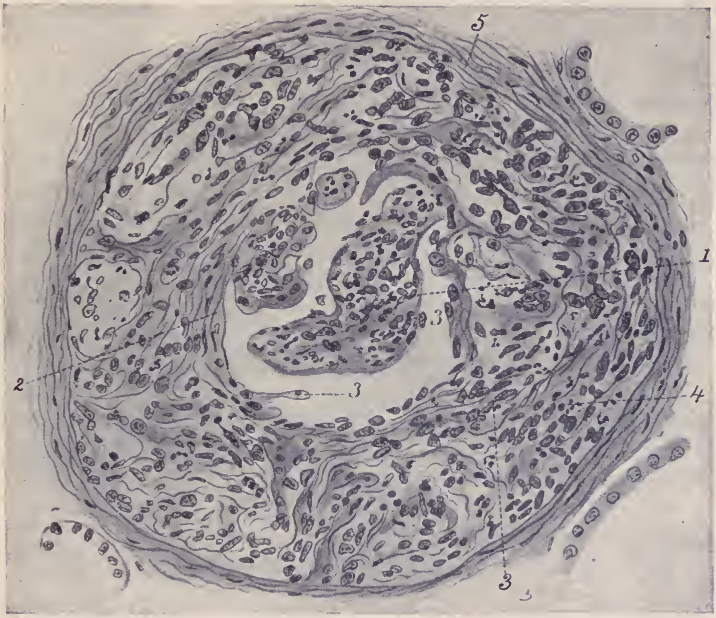

FIG. 166.—CHRONIC GLOMERULONEPHRITIS. × 320 (Dürck).
The capsule fibrillated and thick (5); septa extend inward between the desquamated epithelial cells (3) and leukocytes (4); 2, innermost layer of connective tissue surrounding the greatly diminished tuft (1), which is covered with epithelial cells, the lumen containing leukocytes.

The glomeruli are seldom alone involved, the more common condition being a combination with changes within the tubules.

Ordinarily either of the two preceding varieties terminates in the *acute diffuse nephritis*, a form in which there are exudative or proliferative changes in the interstitial stroma.

The kidney is larger than normal and may be either dark and congested or pale on account of parenchymatous changes. The cortex is much increased in thickness and shows areas of congestion. The capsule strips easily. The microscopic changes are many. The epithelial cells may be cloudy or swollen, show fatty degeneration, or at times be necrotic. Accompanying these changes there may be a well-marked

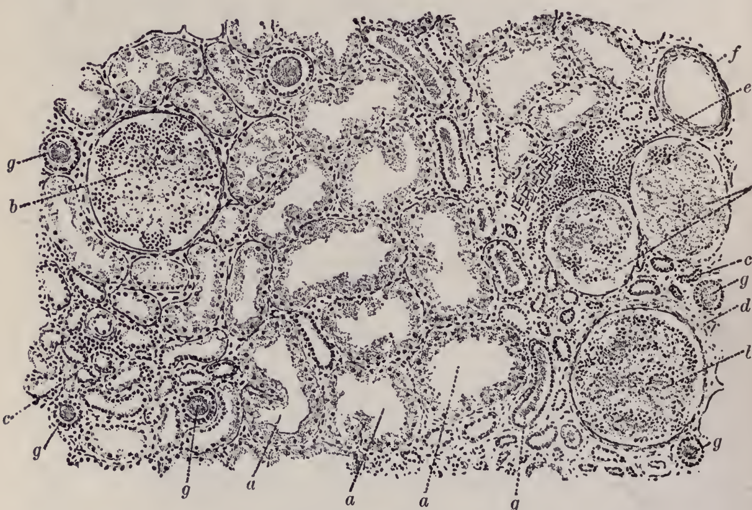

FIG. 167.—CHRONIC PARENCHYMATOUS NEPHRITIS (Kaufmann).
a, Convoluted tubules with cloudy swelling of the epithelium; *b*, glomeruli, more or less degenerated; *c*, atrophic tubules; *d*, sclerotic interstitial tissue; *e*, round-cell infiltration; *f*, blood-vessel; *g*, tube-casts in tubules.

round-cell infiltration in the connective tissue. There may also be small areas of hemorrhage into the tubules or the capsule of Bowman.

The urine is decreased in amount and at times suppressed, has a high specific gravity (1020–1030), due to the large amount of serum albumen present, is dark in color and contains many casts. Microscopically are seen red and white blood-cells, desquamated epithelium, and tube casts, particularly the epithelial and granular forms.

Chronic parenchymatous nephritis may be the result of numerous attacks of acute nephritis, or it may have pursued a chronic course from the outset. It is probably due to the persistent presence in the circulation of some irritating toxic substance. It is characterized by chronic degeneration of the secreting epithelium and by a proliferation of the fibrous connective tissue.

The usual variety is the *large white kidney*, weighing 250 to 300 gm. The kidney is much increased in size, is smooth, pale, and softer than normal. The capsule strips easily. The exposed surface presents a somewhat mottled appearance. On section the cortex is seen to be much thickened, pale and fatty looking, while the pyramids are usually congested and reddish. The cortex may show scattered punctate hemorrhages.

Microscopically the chief change present is a fatty degeneration of the epithelium in the tubules and the glomeruli. The tubules may be filled with granules from the broken-down cells, and erythrocytes may be present. Round-cell infiltration of varying degrees will be found in the interstitial tissues. The Malpighian bodies generally show a proliferation of their epithelium, the capsule of Bowman may become much thickened, and the walls of the capillaries also increase in thickness. The amount of connective tissue is never as great as in the chronic interstitial form.

The urine will contain granular and hyaline casts and varying amounts of albumin.

If the nephritis has existed for a long time, the kidney may become smaller on account of the contraction of the new-formed connective tissue. The organ is then smaller than normal, pale, and granular, the *pale granular kidney*. The epithelium becomes markedly degenerated and the connective tissue contracts and compresses the parenchyma. The capsule is adherent and cannot be removed without bringing away portions of the kidney.

Chronic interstitial nephritis is a form of kidney inflammation characterized by a continual increase in the amount of interstitial connective tissue associated with an atrophy of the secreting cells. Is probably due to the presence within the

blood of an irritant. It is found in alcoholism, syphilis, chronic lead poisoning, and is frequently associated with general arteriosclerosis.

The kidney is small (50 to 60 gm.), dark red in color, firm, and granular, the *red granular kidney*. The irregularities are

FIG. 168.—CHRONIC INTERSTITIAL NEPHRITIS (McFarland).

a, Still functional glomerule with (*b*) mass of newly formed connective tissue surrounding Bowman's capsule; *c*, totally destroyed glomerule; *d*, newly formed cellular connective tissue; *e*, atrophic uriniferous tubules; *f*, slightly altered uriniferous tubules.

due to the contraction of the connective tissue. The capsule strips with great difficulty, tearing away portions of the renal substance with it. On the surface are seen small cysts filled with clear fluid. These are due to the obstruction of a tubule by the pressure of the connective tissue. The tissue

cuts with great difficulty, being almost cartilaginous at times, and presents a typical appearance. The cortex is generally very thin with some places of almost normal thickness. Over the thin areas the capsule is usually considerably thickened. The medulla shows little change.

Microscopically the picture is very definite, although all portions of the kidney may not be equally involved. As the glomeruli are the parts first brought into contact with the circulating toxic substances, it is there, as a rule, that the processes begin. The glomerulus becomes slowly transformed into a more or less homogeneous body that loses all lobulations. At the same time the capsule becomes greatly thickened and the glomerulus is finally transformed into a minute fibrous nodule. The interlobular connective tissue increases until eventually the tubules may become completely atrophic, through compression. Although many of the tubules are atrophic, others will be found markedly dilated, so much so that small cysts may form. There is also a thickening of the walls of the blood-vessels, endarteritis. All these processes may go on to a point where there is very little renal secretory structure left. The parenchyma also shows some changes, but not so markedly as in the chronic parenchymatous variety. There is some atrophy and fatty degeneration.

The urine is generally increased in quantity, of a low specific gravity, 1005 to 1015, with little or no albumin. A few casts of the hyaline and waxy character are found.

Acute interstitial nephritis or *suppurative nephritis* is the result usually of hematogenic infection by micro-organisms, or it may be due to extension of an inflammation of the pelvis of the kidney or of a neighboring tissue. The organisms gain entrance to the kidney as emboli and usually become lodged in the capillaries of the glomeruli. There is an extravasation of round-cells and leukocytes into the capsular space, and into the tissues between the tubules, and minute foci of suppuration are formed. The irritating products soon cause destruction, with necrosis of the adjacent cells. There is generally some extravasation of blood surrounding the areas of suppuration. The process may terminate by the absorption of

the exudate with connective-tissue formation. If the lesion becomes more extensive distinct abscesses may form which may discharge into the tubules or be absorbed and cicatrized.

If the infection has followed a suppurative pyelitis the kidney will be found on section to contain light yellowish colored streaks in the pyramids and medulla. These are composed of tubules that have become filled with pus. Sometimes several of these foci may coalesce and form a larger abscess, which may discharge its contents into the pelvis of the kidney or upon the surface of the kidney; or it may become absorbed and undergo cicatrization. The suppurative process may go on to such a point that the entire kidney becomes converted into a sac filled with pus.

Tube casts are peculiar bodies that are formed within the urinary tubules and that are composed of various albuminoid substances, some of which react like fibrin. *Hyaline casts* are pale, almost transparent, structures reacting like fibrin. They may vary greatly in length and also in thickness; are found most commonly in acute parenchymatous nephritis, but are also present in the chronic parenchymatous and interstitial varieties. The hyaline cast is the foundation of many of the other forms. Its surface is adhesive, and according to the substances upon it, we have *granular*, *epithelial*, *leukocytic*, and *blood* casts. Some blood casts may, however, be formed by the coagulation of extravasated blood within a tubule. *Granular* casts may be dark or pale according to the amount and form of the material composing them. Are found usually in chronic nephritis. The *waxy* cast is a rather large, translucent, and solid appearing body that is found especially in chronic parenchymatous nephritis and in amyloid diseases. At times it may give an amyloid reaction with iodin. *Cylindroids* resemble hyaline tube casts somewhat in general appearance, but are larger and band-like. They are of renal origin and are closely related to true casts.

The effects of nephritis are particularly noticeable in the cardiovascular system when the renal disease is of a subacute or chronic type. There is a hypertrophy of the heart, especially of the left ventricle, which may become greatly

enlarged. The reason for this hypertrophy is not clearly understood. As the kidneys normally secrete urea, chlorids, phosphates, uric acid, urates, and oxalic acid, the accompanying changes may be due to the retention of these substances within the circulation. As in chronic renal disease there is always more or less arteriosclerosis present, the cardiac enlargement may be due to the extra amount of work required to force the blood through the thickened and less elastic vessels. The blood-pressure is usually high, 170 to 220 mm.

The serous membranes in acute nephritis may show inflammatory changes, such as acute endocarditis, acute pericarditis, and pleuritis. *Edema* is particularly common in acute parenchymatous nephritis, especially if the glomeruli and vessels are involved. The edema appears first in the eyelids and hands, but as the disease progresses and the blood-vessels degenerate it spreads over the entire body. Death may result from edema of the lungs. Uremia is also a frequent condition, due probably, to the retention within the circulation of various toxic substances. On account of the retention of such substances there is a decrease of the general vitality, so that the subjects of such a retention are likely to succumb to infections of varying sorts.

Tuberculosis of the kidney may be due to primary hematogenic infection, in which case the condition is usually unilateral, or to secondary involvement following similar disease of other portions of the genito-urinary tract. It may be a part of a general miliary tuberculosis and present numerous minute grayish white tubercles scattered throughout the renal substance, particularly in the cortex. The foci may be surrounded by a narrow zone of congestion.

When there has been an ascending infection from the ureters or a primary local tuberculosis the changes are quite characteristic. The process may begin as a miliary tubercle, which by invasion and lymphatic extension spreads through the organ. The apices of the pyramids are involved and the disease extends through them to the cortex. These areas undergo coagulation necrosis, soften, and eventually dis-

charge their contents into the pelvis of the kidneys, leaving an irregular cavity. On section there are seen numerous large cavities communicating with the pelvis of the kidney. The discharged material infects the mucous covering of the pelvis and the disease gradually extends downward along the ureter until the entire urinary tract may be involved. This,

FIG. 169.—TUBERCULOUS PYELONEPHRITIS (modified from Bollinger)

of course, when the tuberculosis has been primary in character and not due to an ascending infection. The ureter may become obstructed, and the kidney undergo dilatation, thus forming a cold abscess of the kidney, the organ being changed into a sac with thick walls and containing tuberculous pus.

Syphilis is infrequent and not definite in its manifestations.

There have been found gumma giving rise to thick stellate scars.

Tumors of the Kidney.—*Fibromata* in the form of small nodules are occasionally found. *Lipomata* and *leiomyomata* are sometimes encountered.

Fig. 170.—Congenital Cystic Kidney.
Only very small portions of the kidney tissue remain, crowded between the cysts (Delafield and Prudden).

Sarcoma is quite common and is either congenital or else appears, as a rule, very early in life. The tumor may attain considerable size, is usually grayish in color, although it may be red if very vascular, and may be quite soft. Generally the

growth is composed of round or spindle cells, but not infrequently are found fibers of striped muscle, the so-called *rhabdosarcoma*. Such growths are really mixed embryonic tumors resulting from cell inclusion, possibly of the Wolffian body. Sarcoma may occasionally be found in later life. Such a tumor differs from the congenital form in being slow in growth and not giving metastases until late. The congenital form is rapidly malignant and destructive.

Of the tumors of epithelial type, although of mesodermic origin, the *hypernephroma* is the most common. It is derived from portions of adrenal tissue that have been included within the kidney during its development. The structure of the tumor resembles that of the adrenal gland, except that the cortical elements are the more prominent. Adrenal rests very seldom contain any medullary tissue. The neoplasm may be small and remain circumscribed, or it may take on a rapid growth and become destructive, giving metastasis through the blood-vessels. The cells contain fat and glycogen.

Adenoma is rare. It occurs as small, circumscribed nodules composed of glandular alveoli, which may show papillary outgrowths and also at times be cystic. Occasionally it becomes malignant.

Carcinoma as a primary growth is unusual and secondary metastases are not common. The secondary form makes its appearance as small scattered nodules. The carcinoma may become quite large, and destroy the renal tissue, and is frequently associated with hemorrhages into the tissue.

Cysts of the kidney are quite common and are of various forms. They may be single or multiple, large or small. In the majority of cases they appear as numerous small collections of fluid scattered over the surface of the kidney. They are simple retention cysts due to the obstruction of the tubule below the glomerulus; are especially common in chronic interstitial nephritis. Occasionally a kidney may contain a single large cyst and otherwise be apparently normal. Is probably due to the obstruction of a tubule.

The kidneys may be congenitally cystic, and in such a case present a characteristic appearance. Both kidneys are gen-

erally affected and are filled with numerous cysts, some of which may be as large as a walnut. These may be filled with a urinous or even a colloid material, and are separated from each other by a very thin stroma of connective tissue. They probably result from a failure in the accurate joining of the urinary tubules (nephrogenic tissue) with the outgrowths of the Wolffian duct. The organs may be very much enlarged. Generally such a condition is incompatible with life, but similar lesions may be found in adults. As long as the remaining renal substance is able to maintain the excretion the individual will live, but when the organs become incompetent, death may ensue from uremia.

Hydronephrosis is a cystic dilatation of the kidney resulting from an obstruction of the ureter. Is more likely to occur if the obstruction is of an intermittent character. When the ureter is obstructed, as by a calculus, by inflammatory changes, by twists or kinks, or by pressure from new growths either within or similar conditions on the outside, it and the pelvis of the kidney will begin to dilate. The urine, being unable to escape, collects and gradually causes the tissues to stretch. The pelvis becomes larger, the calices are flattened out, and the renal tissue becomes atrophic until, as a result of the combined pressure and atrophy, there is a mere shell of kidney substance remaining. The fluid contained within the sac is at first practically normal urine. As long as there is any secretory tissue left, urine is excreted, but when that ceases, the salts in the fluid are either precipitated or absorbed and the remaining liquid is watery. Such cysts may become infected or hemorrhages may take place within them. When filled with pus, the condition is known as *pyonephrosis*.

Nephrolithiasis.—*Renal calculi* are quite frequently found in the pelvis of the kidney and are composed of material precipitated from the urine. They may occur in the form of fine particles like sand or they may be so large as to be unable to pass out through the center. When small, the calculi can pass from the kidney without giving any pain. As they become larger they may pass out and give rise to severe renal colic; if quite large, the ureter may be completely blocked, and

dilatation and atrophy follow. The concretions may also vary in shape, some being round and smooth, while others may be very rough, and if large send prolongations into the calices. The commonest variety is composed of uric acid and oxalate of lime, but phosphatic stones are found occasionally. The color varies according to whether uric acid and urates or the phosphates predominate.

The presence of calculi may cause degeneration and atrophy as a result of pressure, and suppuration is quite common. Obstruction of the ureter gives rise to varying degrees of hydronephrosis.

The presence of calculi seems occasionally to antedate the formation of a carcinoma.

DISEASES OF THE URETER

There may be obstructions due to congenital atresia or to various diseases and neoplasms. The result of such a condition is a dilatation of the ureter above the obstruction and of the kidney (hydronephrosis).

Pyelitis, or inflammation of the pelvis of the kidney, is met with in the course of various infectious diseases, as typhoid fever, scarlet fever, smallpox. In such cases is seldom of any severity. The most important causes are local infection and calculi. Infection may take place through the presence of pyogenic organisms within the urinary apparatus, and according to the degree of severity the inflammation may be catarrhal, hemorrhagic, suppurative, pseudo-membranous, or ulcerative. In the suppurative form there is nearly always an involvement of the renal tissue, a *pyelonephritis*. If the ulcerated form is severe, perforation may take place and the purulent contents escape into the surrounding tissue, giving rise to a *perinephritic* abscess, the pus collecting in the areolar and fatty tissue about the kidney. It may remain encapsulated, and compress the kidney, or it may burrow through the deeper tissues and discharge below Poupart's ligament.

In chronic pyelitis the mucous membrane may become much thickened, contain ulcerations, and be covered in places

by a precipitation of the salts from the urine. The kidney in this form is often the seat of chronic inflammation, suppuration, or atrophy.

If the ureter becomes obstructed, the pelvis of the kidney may be filled with pus, a *pyonephrosis.*

Tuberculosis of the ureter occurs as a rule secondarily to tuberculosis of the kidney, but it may have followed similar disease of the lower portion of the urinary tract.

FIG. 171.—TUBERCULOUS NODULE IN THE WALL OF THE URETER, WITH BEGINNING HYDRONEPHROSIS (from a specimen in the Museum of the Philadelphia Hospital, Phila.).

Calculi may lodge within the ureter and give rise to varying disturbances, from acute renal colic to obstruction with subsequent hydronephrosis. Hemorrhage may be caused by laceration of the mucous membrane and suppuration is not uncommon.

Parasites at times find their way into the ureters and pass up to the kidney.

DISEASES OF THE BLADDER

Malformations of the bladder are quite common. The most usual form is a lack of union along the anterior median line with failure of closure of the abdominal wall, *exstrophy* of the bladder. Is usually associated with epispadias, or with division of the clitoris. Occasionally there may be a communication with the rectum or the vagina. Sometimes there is no urethra.

The urachus may remain patulous and urine be discharged at the umbilicus or may be retained in the anterior abdominal wall as a cyst. Diverticula may occur, usually in the anterior wall. The bladder may be completely lacking, the ureters emptying directly into the urethra, or the organ may be divided into two portions by a septum.

Hypertrophy of the bladder may follow any chronic interference to the outflow of urine. The muscular coat of the wall becomes much thickened and the mucous membrane also increases in thickness and is thrown into folds. Indications of chronic inflammation are also usually present.

Dilatation of the bladder may be congenital or acquired. It is due either to obstruction to the escape of urine or to paralysis of the muscular coat of the wall. As a rule, the condition results from long-continued interference with the escape of urine, and is accompanied by a hypertrophy of the walls with thickening of the mucosa. The fibrous bands are prominent and the mucosa in between is pouched. Diverticula are quite frequent. If the dilatation has taken place suddenly, as in paralysis, the vesical walls are very thin. Such a weakening is often accompanied by rupture, with peritonitis.

The bladder may occupy an abdominal position, particularly in women, when there has been some laceration of the perineum. Its walls may prolapse into the vagina, forming a cystocele. At times it may be completely inverted.

Rupture of the bladder may follow severe injury or acute dilatation. The rupture generally occurs at the base and is followed by peritonitis and death. As a result of traumatism the injury commonly occurs near the neck of the bladder and

is followed by extravasation of urine into the surrounding tissue, which generally gives rise to a severe phlegmonous cellulitis.

Fistulous communications with the vagina or rectum are not uncommon in women as a result of injuries received during childbirth.

Circulatory Disturbances.—*Active hyperemia* is usually dependent upon infection by some micro-organism or due to the presence in the urine of irritating substances. The mucous membrane is diffusely red.

Passive hyperemia is due to thrombosis of or pressure upon the inferior vena cava. Occurs also in cirrhosis of the liver. The mucous membrane is dark red in color, the vesical veins at the neck of the bladder become distended and varicose, and there is some catarrhal inflammation. Severe hemorrhage may occur from a rupture of one of the varicose veins or the veins may be the seat of thrombosis.

Hemorrhage may be caused by injuries, calculi, malignant disease or result from ruptured varicose veins.

Inflammation.—*Acute cystitis*, inflammation of the bladder, may be due to the presence of pus-producing organisms, to the colon bacillus and the gonococcus, that have gained entrance from the urethra or to the presence of irritating substances within the urine. The infecting agent may have been introduced by the use of unclean instruments in catheterization. The bladder is usually empty or else contains a small amount of cloudy urine that throws down a sediment composed of desquamated epithelium, mucus, pus cells, and bacteria. The mucosa is hyperemic, swollen, and edematous. The process may subside in a short time or it may become *pseudomembranous*. The inflammation extends into the deeper tissues, necrosis of the epithelium with ulceration takes place, and over these areas is formed a pseudo-membrane. The greater part of the vesical walls may be thus covered.

Phlegmonous cystitis may be a further stage of the above processes, but it usually results from a rupture of the bladder. The vesical walls and the surrounding tissues become infected and are the seat of abscess formation.

Chronic cystitis may follow acute inflammation, but is generally caused by some chronic obstruction to the escape of urine, such as an enlarged prostate or a stricture. As a result of obstruction there is a retention of urine, with subsequent infection. Decomposition follows and the irritating products set up a chronic inflammation. The mucous membrane becomes much thickened and even polypoid, is reddened, and frequently ulcerated. Lime salts may be deposited in the degenerated tissues. The muscular fibers hypertrophy, but they gradually lose their strength and the urine is not discharged. Hemorrhages into the vesical walls are common.

As a result of injuries to the spinal cord the bladder may undergo a rapid dilatation and the walls at the same time have their nutrition interfered with. The urine rapidly collects, undergoes fermentative processes, and causes necrosis of the mucous membrane. This may be followed by perforation with fatal peritonitis and at times gangrene.

Tuberculosis of the bladder is generally secondary to tuberculosis of the epididymis, seminal vesicles, or prostate, or occurs as a descending infection from disease of the kidney. The disease manifests itself in the form of ulcers that are commonly located in the trigone, from which they may extend upward, involving the lower half of the bladder. The involved areas undergo cheesy degeneration and are frequently the seat of a deposit of urinary salts. There is usually a chronic cystitis present. Tuberculosis of the bladder is very much more common in men than in women. Primary tuberculosis is extremely rare and *syphilitic* ulcers are also very unusual.

Vesical calculi are very frequently encountered. They are composed of substances normally or abnormally present in the urine. They may be present in great numbers, when they are small, like fine particles of sand, or singly as one large stone several centimeters in diameter and weighing as much as 1000 gm. The shape and the general characteristics of the calculi depend upon the material of which they are formed. The stones may be imbedded within the mucosa or they may lie free within the bladder. In the latter case

the sides of the stones may be worn smooth by mutual contact.

The formation of a stone is generally considered to be due to the precipitation of the various salts about some desquamated epithelium or foreign body. This is accompanied by a coagulation of albuminous material about the calculus and

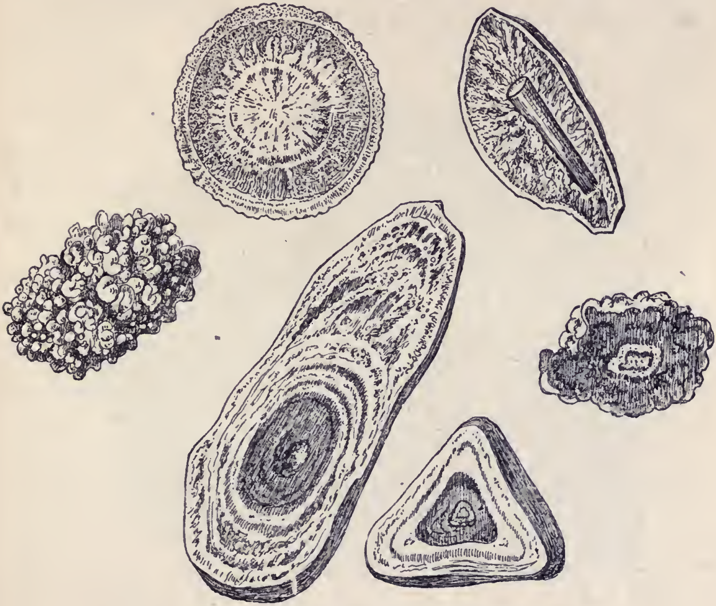

FIG. 172.—URINARY CALCULI (Orth).

Showing the nuclei from which they originate, the concentric laminæ by which they are formed, the radiating infiltration sometimes observed, and the various smooth and nodular surfaces.

then another layer of mineral salts, giving a distinctly laminated appearance to the stone. Occasionally the nucleus may be a renal calculus that has passed through the ureter. It is usually of a different composition than those formed within the bladder.

Associated with the formation of calculi is generally a retention of urine.

These stones may be made up of uric acid or urates, of oxalate of lime, of phosphates, of carbonate of lime, or of various organic bodies, as cystin or xanthin.

The characteristics of the various calculi are as follows:

1. *Uric acid*, are less common in the bladder than in the kidney. Are small, round, hard, slightly granular surface, of a yellowish, reddish, or brownish color. They probably originate within the kidney.

FIG. 173.—PAPILLOMA OF THE BLADDER. × 35 (Ziegler). Section through a tuft.

2. *Urates*, of ammonium magnesium, often are covered by earthy phosphates. May be as large as a hen's egg, oval, smooth surface, pale in color, and laminated. If composed entirely of ammonium urate are seldom larger than a pigeon's egg, rounded but also flattened, friable, granular, and dull yellow.

3. *Calcium phosphate*, medium-sized, irregular surface, grayish in color, hard and brittle, or soft and crumbling if there is much triple phosphate present. Frequently form about small uric acid calculi.

4. *Triple phosphates*, large, irregular, grayish, soft, and friable.

5. *Carbonate of lime*, are rare, are small, white, and chalky.

6. *Oxalate of lime*, are round, brownish color, surface irregular and nodular, very hard, may be quite large. Are the *mulberry* calculi.

7. *Cystin*, unusual, small, oval, brownish or greenish, soft and waxy.

8. *Xanthin*, very rare, small brownish, smooth surface, and brittle.

Results of the vesical calculi are many. Their presence may cause obstruction to the outflow of urine, with subsequent dilatation of the bladder and its accompanying chronic cystitis. By pressure, atrophy and ulceration of the mucous membrane may take place, with even perforation. Hypertrophy of the vesical walls occurs. There are frequent attempts at micturition, accompanied by straining and tenesmus, with frequent bloody urine. If long continued the obstruction may give rise to bilateral hydronephrosis or pyonephrosis if the infection extends upward.

Sometimes the calculus may become lodged in a pouch of the wall and become completely encapsulated.

Tumors.—*Polypoid* thickenings of the mucosa are quite frequently found in chronic inflammations of the bladder. *Papillomata* generally appear as small villous outgrowths, covered by epithelium. Are very vascular and may give rise to such considerable hemorrhage that grave or fatal anemia ensues. Occasionally bits of the papillary growths may break off and be passed through the urethra or they may be large enough to cause obstruction. These tumors are benign, but there is a possibility of their becoming malignant. True connective-tissue tumors, particularly sarcoma, are rare. *Carcinoma* in the form of a squamous epithelioma is an infrequent primary tumor. It occurs as a cauliflower mass that frequently undergoes ulceration. The neighboring organs are generally involved by contiguity. Secondary *carcinoma* may follow malignant disease of the sexual organs, of the rectum, or of the prostate by direct extension. The

bladder is very rarely the seat of a metastatic growth. Cysts very rarely are found.

DISEASES OF THE URETHRA

Malformations.—Occasionally the urethra may be absent, or the superior or inferior walls may be incomplete, giving rise to epispadias and hypospadias respectively.

Inflammation.—*Urethritis*, inflammation of the urethra, is nearly always an infectious condition resulting from the presence of the gonococcus. Non-specific urethritis may be due to injuries or to the entrance of pyogenic micro-organisms. In gonorrheal urethritis the mucosa of the anterior urethra is first involved. It becomes red and swollen and there is soon a formation of pus accompanied by a desquamation of the epithelium. In the pus cells as well as in the epithelial the characteristic organisms will be found. There is generally an infiltration into the deeper layers of the mucosa by the gonococci. The infection may extend to the posterior urethra, and involve the bladder, epididymis, prostate, seminal vesicles, and in women the bladder, vagina, uterus, and Fallopian tubes.

The inflammation in the urethra may subside without doing any damage or it may set up infectious processes in other parts of the body. Is not uncommon to have a gonorrheal ophthalmia, gonorrheal arthritis, an acute endocarditis, or pericarditis.

The acute form of urethritis is often followed by a *chronic* inflammation called *gleet*. The posterior urethra is the part generally involved and is accompanied by a very slight discharge of a thick transparent mucus seen in the morning. Not infrequently a fibrous cicatrix is formed in the urethra. This undergoing contraction gives rise to a stricture which is most commonly located in the membranous portion. If the narrowing is severe, the urine may be prevented from escaping, and consequently cause a dilatation of the bladder with hypertrophy and chronic cystitis. The ureters and kidneys may even be involved.

Injuries.—The urethra may be the seat of various injuries resulting from direct trauma, external or internal. If

it is completely lacerated urine is able to escape into the tissues and rapidly give rise to a suppurative or gangrenous cellulitis. This may be very widespread, including the lower half of the abdomen and the upper part of the thighs. Fistulæ communicating with the vagina or rectum or opening externally may be formed.

Tuberculosis and **syphilis** are rare.

Tumors of the urethra are unusual except when secondarily involved by a neoplasm in adjacent structures, as in squamous epithelioma of the glans penis or in carcinoma of the prostate; in women in cancer of the cervix. The urethral *caruncle*, found in the meatus in women, is a fibrous angioma. Sarcoma, myxoma, and fibroma sometimes occur.

CHAPTER XXIII

DISEASES OF THE REPRODUCTIVE SYSTEM

MALE ORGANS

THE PENIS

Malformations of the Penis.—The penis may be absent, undeveloped, or, what is very rare, double. There may be lack of closure of the urethra on the dorsal surface, *epispadias*, or, on the under side, *hypospadias*. In the latter condition the cleft may extend posteriorly and separate the scrotum into two lateral halves. This is usually the condition in the cases of hermaphrodism. Epispadias may be associated with exstrophy of the bladder. The prepuce may be absent or, what is quite common, elongated and the orifice greatly narrowed; is termed *phimosis*.

Inflammation of the glans penis is known as *balanitis*, of the prepuce as *posthitis*, of the two together as *balano-posthitis*. Is generally the result of uncleanliness. Is a quite common complication in phimosis when the prepuce cannot be retracted. The smegma and urine undergo decomposition and set up an inflammation; infection, as in gonorrhea, may be the cause. Occasionally the prepuce when inflamed may be retracted behind the glans and unable to be drawn forward. Is called *paraphimosis*, and by its constriction may give rise to serious secondary conditions.

Injuries to the penis may give rise to hemorrhage or to rupture. If it becomes infected suppuration and gangrene may result. If the urethra has been lacerated extravasation of urine with its accompanying symptoms may occur. Injuries are likely to be more severe when the penis is in an erect condition.

Tuberculosis is rare. It appears as ulcerations on the glans with cicatrization and necrosis.

Syphilis generally makes its initial appearance on the penis as the true chancre.

Tumors of the penis are frequently found and are generally epithelial in structure. The *papilloma* or *condyloma* appears as a hard, rough, cauliflower-like growth upon the glans penis or prepuce. Is composed of vascular connective-tissue villosities covered by squamous epithelium. *Carcinoma* usually occurs in the form of the squamous epithelioma arising from the glans or the prepuce. It is generally warty and prone to ulcerate. Large areas of the penis may be destroyed and metastases to the neighboring inguinal lymph-nodes occur. The connective-tissue tumors are rare.

Scrotum.—Is quite frequently the seat of epithelioma in chimney-sweepers and paraffin-workers. *Elephantiasis* is common in the East and in many cases is due to the filariæ. The subcutaneous tissue is greatly increased, so that an extreme enlargement may occur. *Dermoid cysts* are occasionally met with.

THE TESTICLES

Malformations.—One or both testicles may be absent or hypoplastic. *Cryptorchia* is a condition in which one or both testicles instead of descending into the scrotum remain within the abdominal cavity or in the inguinal canal. Occasionally the testicles may not descend till puberty. The undescended testicles are usually small and imperfectly developed, and are not uncommonly the seat of a sarcomatous proliferation.

Atrophy of the testicle occurs in senility and after chronic inflammations. The organ is small and dense, is dark in color, and is incapable of spermatogenesis, the epithelium having undergone a fatty degeneration.

Hypertrophy has been noticed as a compensatory change following the removal of one testis and is characterized by an increase in size of the seminiferous tubules.

Fatty degeneration is quite frequently observed as a result of pressure from tumors or from other pathologic conditions within the testicle.

Inflammation of the testes—*orchitis*—and of the epididymis—*epididymitis*—are commonly encountered. The two may occur together or alone. If the surrounding tunica albuginea is involved the condition is called *periorchitis*.

The inflammation may be due to traumatism or to infection, the latter usually resulting from the extension of a gonorrhea. In typhoid fever, scarlet fever, syphilis, smallpox, and mumps the testicles are occasionally the seat of inflammatory changes, as a result of hematogenous infection. The traumatic and gonorrheal processes generally involve the epididymis only.

Orchitis may be acute or chronic. In the acute form the testicle is swollen, hard, and very painful on account of the organ being inclosed within the fibrous tunica albuginea. Microscopically there is seen a marked round-cell infiltration between the tubules. The epithelial cells degenerate and desquamate. The condition may terminate in suppuration; and if the tunica is broken through, the testicular substance may protrude and form a fungous condition. The organ may, on the other hand, entirely recover.

Chronic orchitis usually follows the acute variety or as a complication of syphilis. In it there is a great hyperplasia of the intertubular connective tissue with subsequent contraction, atrophy, and degeneration, the testicle becoming very dense.

In *epididymitis* that structure becomes much swollen and painful and is usually associated with a serous exudation into the tunica vaginalis.

Tuberculosis generally is primary in the epididymis and secondarily involves the testicles. The infecting organisms may gain entrance either through the circulation or from the urethra through the vas deferens. In the latter form there has generally been a pre-existing tuberculosis of the seminal vesicles, prostate, or bladder.

The condition is, as a rule, secondary to pulmonary tuberculosis, small tubercles develop, these increase in size, coalesce, and form quite large caseous masses which may break down and rupture externally. The interstitial tissue may be more

or less densely and diffusely infiltrated by small round cells. The epithelium lining the tubules may be fatty and degenerated. The walls of the tubules may be much thickened by a round cell infiltration.

Syphilis, either acquired or congenital, may give rise to changes in testicles and epididymis; the testicle usually being involved secondarily. There is generally an intertubular round-cell infiltration with induration and degeneration of the tubular epithelium. Gummata sometimes form and undergo a caseous degeneration with subsequent cicatrization.

Leprosy of the testicle in the form of nodular formations, with degeneration and atrophy of the tubules, has been noted.

Tumors.—*Fibroma*, *lipoma*, and *myxoma* are sometimes encountered. *Chondroma* and *rhabdomyoma* have been described. *Sarcoma* in all varieties occurs in the testicle, less commonly in the epididymis. Secondary changes frequently occur, and cysts of various sizes may form as a result of the obstruction of the seminiferous tubules. Combinations of the sarcoma with chondroma, lipoma, fibroma, etc., are quite common.

There have also been described tumors of the testicle that contain areas resembling the *chorioepitheliomata* that are found in women. Typical syncytial, Langhan's, and wandering chorionic cells being found in some cases.

Adenoma is rare; when present it is generally associated with carcinomatous proliferation of the epithelium. *Carcinoma* is not unusual, and though usually medullary in type, may be scirrhus. Is frequently associated with cystic dilatations of the tubules. Various degenerations, as mucoid and colloid, are quite commonly seen. Although the tumor originates within the cells of the seminiferous tubules of the testicle the epididymis and vas are soon involved, the entire organ being transformed into carcinomatous tissue. The inguinal and lumbar lymph nodes are involved frequently and distant metastasis may occur.

Cysts.—*Spermatocele* is the term applied to a cystic dilatation of a seminal tubule, usually at the head of the epididymis. It may be quite large, containing up to 350 c.c. of a watery,

slightly turbid fluid in which spermatozoa, either active or dead, may be found. *Retention* cysts may occur as a result of inflammatory changes, or to obstruction of the tubules by some new growth. *Dermoid* cysts are rarely found.

Vaginitis testis, or **periorchitis,** is an inflammation of the tunica vaginalis. It occurs as a result of inflammation of the testicle or epididymis, in the course of various infectious diseases or in consequence of traumatism. The most common form is the *serofibrinous* variety in which there is an accumulation of serous fluid within the tunica vaginalis, giving rise to a *hydrocele*, usually unilateral. The process may continue slowly and the tunica be tremendously distended by a clear straw-colored fluid. In acute cases the fluid may be purulent or hemorrhagic.

If the hydrocele has continued a long time the tunica vaginalis becomes much thickened and the testicle and epididymis frequently atrophic.

THE SEMINAL VESICLES

Vesiculitis, or inflammation, generally follows an attack of gonorrhea or of prostatitis. The tubules become dilated by a mucopurulent exudate, are congested and tender, and in chronic inflammation, there may be a connective-tissue formation. This through contraction may give rise to various deformities. Obstruction to the tubules as they enter the prostatic tissue causes the dilatation.

Tuberculosis may be primary or secondary to tuberculosis of the pulmonary or genito-urinary tracts. The bacilli gain lodgment by means of the blood-vessels or lymphatics. They are present in the semen and when contained within the vesicles infect them.

Tumors are seldom primary, usually being secondary to carcinoma of the prostate or rectum.

THE PROSTATE GLAND

Atrophy of the prostate is common in old age, the gland becoming smaller through degeneration of the epithelium with contraction of the fibrous tissue.

FIG. 174.—HYPERTROPHY OF THE MIDDLE LOBE OF THE PROSTATE (White and Wood).
A, Middle lobe of prostate; *B*, urethra.

Hypertrophy also frequently occurs in old men. The entire gland or any one of its lobes may increase in size. Although the gland is composed of two lobes connected by a narrow isthmus the hypertrophy can involve the isthmus alone and cause a great increase in size. The median enlargement is the most important, as it is the one in which

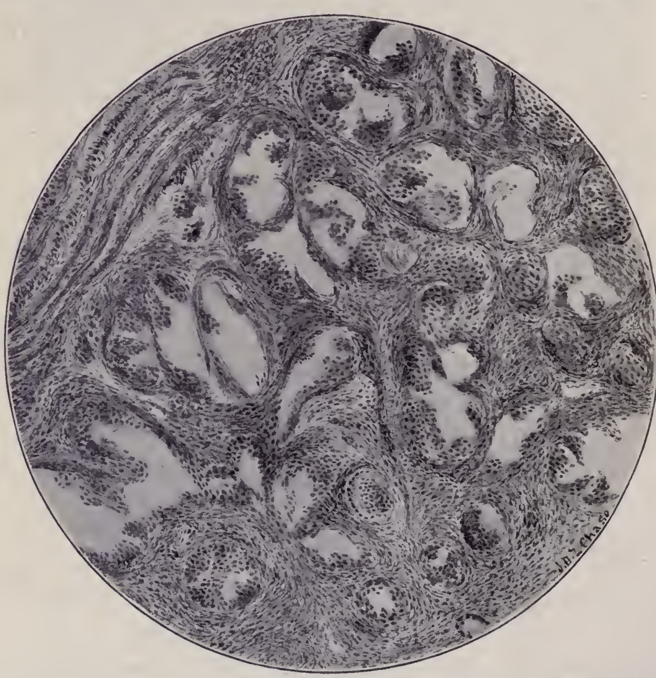

FIG. 175.—HYPERTROPHY OF THE PROSTATE GLAND (McFarland).

there are severe clinical symptoms. By the hypertrophy of this portion the opening to the urethra is obstructed and retention of urine occurs. This may at first merely give rise to increase in the thickness of the muscle-fibers and dilatation of the bladder. Subsequently infection takes place, the urine decomposes, and the bladder is no longer able to expel the urine. Pyelitis and pyelonephritis may follow.

Microscopically the enlargement is due either to a glandular increase or to a hyperplasia of the fibrous connective-tissue stroma and the muscle. In the latter case there may be more or less widespread atrophy of the tubules. In the glandular form the appearance closely simulates that of an adenoma.

The enlargement may result from a chronic posterior urethritis or a long-continued congestion.

Prostatitis, inflammation of the prostate, is nearly always secondary to a gonorrheal posterior urethritis, but may follow injury to the perineum. In the acute infectious form there is a desquamation of the glandular epithelium, with collections of pus in the acini, and a round-cell infiltration of the interstitial tissue. There may be numerous foci of suppuration scattered throughout the tissue. Large abscesses may form and these generally evacuate into the urethra. If further infection of the surrounding tissues does not occur cicatrization and recovery take place.

With the opening into the urethra there may be an extravasation of urine with phlegmonous inflammation of the pelvic tissues.

If the abscesses do not rupture, they may be absorbed or become inspissated, encapsulated, and calcified.

Concretions are quite frequently found in the prostatic alveoli in old men. They are generally numerous and vary in size from the microscopic to those large enough to be seen with the naked eye. They are round, translucent, colorless bodies that show a distinct concentric arrangement. The older ones are of a slight brownish tinge. They are frequently spoken of as *corpora amylacea* on account of their so often giving a starch reaction, coloring blue or a mahogany-brown color with iodin. They may, however, not stain at all. As they become larger, lime-salts are commonly deposited around them. Occasionally the concretions may be so large as to cause the ducts to dilate. At times they escape into the urethra and are passed out with the urine.

Tuberculosis of the prostate is generally secondary to tuberculosis of the other genito-urinary structures, particularly of the vas deferens and epididymis. Throughout the gland

there are caseous masses varying in size. These may become encapsulated and calcified or may rupture into neighboring tissues. Primary tuberculosis sometimes occurs as a hematogenic infection, but is quite rare.

Tumors of the prostate are not common. *Sarcoma* and *adenoma* are very rare. *Carcinoma* is more frequent, but even it is unusual either as a primary or a secondary growth. It may occur in rather young individuals and appears as a nodular yellowish mass that projects into the bladder and urethra. It soon breaks down, leaving an ulcerated surface. Extension usually involves the bladder and rectum, but metastases to the inguinal nodes or more distant organs frequently take place; death rapidly ensuing.

Cysts are very rare, occasionally arising from remnants of Mueller's ducts or from obstruction to the ducts.

COWPER'S GLANDS

These become involved in the course of inflammations of the prostate gland or of the urethra. The glands become hyperemic, enlarge, and may suppurate. The abscess may rupture into the urethra or externally, in either case giving rise to a fistula. The duct may become narrowed as a result of inflammation and form a retention cyst.

THE FEMALE ORGANS

THE OVARIES

Malformations.—The ovaries may be hypoplastic or occasionally one may be absent, seldom both. An ovary may be much displaced, sometimes being found in the inguinal canal or in the labium majus. It may also be displaced as a result of a change of position in the uterus or from pressure or adhesions.

Circulatory Disturbances.—*Active hyperemia* may be either pathologic or physiologic; in the first as a beginning inflammation or in the latter during the menstrual period.

Chronic hyperemia is found in chronic heart disease or as a result of some localized obstruction.

Hemorrhage takes place when a follicle is ruptured. The blood escapes into the follicle after the ovum has been cast off and at the same time the cells lining the follicle proliferate. They soon undergo fatty degeneration, forming the *corpus luteum* of menstruation. The blood is finally absorbed, the cells break down, and organization takes place, leaving a small scar. When impregnation has occurred the corpus luteum is considerably larger than the above, and there is a more marked proliferation of the follicular cells. Instead of rapidly organizing it may persist even to the end of pregnancy. It contains a translucent gelatinous substance and little blood. The luteal cells are arranged in peculiar fan-like folds.

Oöphoritis, or *inflammation* of the ovaries, is generally secondary to an inflammatory condition of the Fallopian tubes or of the peritoneum. Is generally due to the presence of pyogenic organisms which may infect the ovary by direct contact, as in peritonitis, or be carried in the blood- or lymph-vessels.

The ovary is much enlarged and congested and round-cell infiltration is common. Small abscesses may appear as minute yellowish points. Occasionally larger collections of pus form and these may rupture into the peritoneal cavity or into a loop of intestine. Generally the inflammation quiets down with absorption or inspissation of the abscesses and terminates in connective-tissue formation, *chronic oöphoritis*. As a gradual transformation of the ovary into fibrous tissue is a normal process as the person advances in age, the change cannot always be attributed to inflammatory processes. The walls of the blood-vessels are usually much thickened and may show hyaline changes.

Adhesions frequently follow oöphoritis and may cause serious trouble by their presence.

Tumors of the ovary are, as a rule, cystic in character.

Small follicular cysts may occur singly or multiple, as a result of the failure to discharge the ovum, with subsequent enlargement of the follicle. They may become as large as a man's fist and contain a thin or jelly-like fluid that is usually clear but which may be discolored by the presence of blood.

Such cysts are lined by a single layer of flattened epithelium, and are formed within the ovarian tissue.

The neoplastic cysts differ from the follicular in that the dilated spaces are surrounded by fibrous tissue that supports a vascular basement membrane upon which the cells rest. The epithelium is usually columnar and rarely is ciliated. These cysts are probably developed from Pflüger's tubes, and represent a *cystic adenoma*.

Instead of being single they are multilocular, and may be divided into two groups—the simple cystoma and the papillary cystoma. The material contained within the cysts is usually clear and gelatinous, if there has not been an admixture of blood. Although this substance closely resembles mucin it is not precipitated by acetic acid, consequently it is known as *pseudomucin*.

The *simple cystoma* is a benign growth and retains to some extent a glandular arrangement, in that there are formed acini lined by epithelium. It is usually multilocular, although in many instances the septa between the acini have been broken. The contents are usually thick and viscid on account of the pseudomucin present and vary from transparent to a reddish or even chocolate color. This substance is less frequently found in the papillary cystoma.

At times the proliferation of the epithelium may take on a malignant tendency and give rise to a carcinomatous degeneration. This is more frequent in the papillary variety.

The *papillary cystoma* are generally bilateral and probably originate from the paroöphoron. From the inner surface of the cyst there extend papillary outgrowths covered by a stratified layer of ciliated columnar epithelial cells, many of which are of the goblet type. The fibrous framework is less marked, and concentric calcareous bodies (psammoma bodies) may be found within it. The substance in these cysts resembles that found in the simple form, except that there is a less amount of pseudomucin.

This form is much more inclined to undergo a secondary malignant degeneration than is the simple cystoma. The growth may be so rapid as to cause the wall of the cyst to

rupture and the papillary structures project on the surface, giving rise to a cauliflower-like mass.

Dermoid cysts are more commonly found in the ovaries than in any other part of the body. They may be very small or large, and though generally unilateral may occur in both ovaries. Their structure and origin has already been described.

FIG. 176.—PAPILLARY CYSTOMA OF THE OVARY. × 150 (Ziegler).

Their origin has been explained as a *fœtus in fetu*, or as a result of parthenogenesis of an unfertilized ovum.

Carcinoma of the ovary is nearly always a primary growth. It is glandular in character and generally undergoes a mucous degeneration. It usually gives a widespread metastasis along the peritoneum. Is not infrequent in childhood, and is rapidly fatal.

Fibroma may be found singly or multiple. They probably originate from the scars formed in the organization of the

corpora luteii. Combination with sarcoma, fibrosarcoma, sometimes occurs. *Myofibroma* are also met with. *Chondroma* is rare. *Sarcoma* is rare, but may occur as a spindle cell or, more rarely, as a round-cell variety. Myxomatous degeneration is common. Metastasis is unusual, and the malignancy of these growths is slight. If there are many glandular structures present the neoplasm is called an *adenosarcoma*. *Angiosarcoma* occasionally occurs. *Endothelioma* is unusual.

THE FALLOPIAN TUBES

Malformations of the tubes are not frequent. Are usually associated with abnormalities of the uterus. They may occupy unusual positions as a result generally of adhesions.

Hyperemia of the tubes occurs in the early stage of inflammation and during menstruation. *Hemorrhage* is rare, except from a rupture of the tube in an ectopic pregnancy.

Salpingitis or inflammation of the tube is always the result of infection by micro-organisms gaining entrance from the uterus. It may be acute or chronic, and the most common cause is the gonococcus. Is also generally present in puerperal infections.

In the *acute* form the mucous membrane of the tube shows a catarrhal inflammation with an accompanying exudation, this latter varying according to the severity of the inflammation, being mucous, purulent, or hemorrhagic. There is a marked round-cell infiltration of the mucosa, and many of the epithelial cells may desquamate.

The exudate escapes from the fimbriated end of the tube, and sets up an inflammation of the adjacent tissues with the formation of adhesions. If the uterine end becomes obstructed the exudation may be retained. If the contents are purulent a *pyosalpinx* is formed; if much blood is present, a *hematosalpinx;* and when serous, the condition is called a *hydrosalpinx*. If the secretion of fluid continues the tube may become much dilated with any of the above contents. The walls will become thinner and rupture may occur. The contents may be discharged into the abdominal cavity, into the intestine, or

be walled in by adhesions. If rupture occurs during the acute stage general peritonitis will usually result. If, however, the condition has been chronic the exudation is nearly always sterile on account of the death of the infecting bacteria.

In *chronic* salpingitis there is a hyperplasia of the connective tissue and muscularis; it is generally secondary to an acute infection. The tube-walls become much thickened, and adhesions to the outer surface are present. They may cause considerable distortion.

The contents of the tube may gradually be absorbed or calcareous material may be deposited.

Tuberculosis of the tubes is unusual; it may be either primary or secondary. The general appearance is similar in both forms. On the surface are numerous scattered miliary tubercles, and throughout the walls of the tube are minute caseous areas. Dense adhesions are commonly formed, and the organs are firmly bound down to neighboring structures. This condition may be associated with gonorrheal salpingitis. The uterus may become secondarily involved by the discharge into it of infected material from the tubes.

Syphilis is very rare, but has been found in the form of gummata and connective-tissue hyperplasia.

Tumors are not very frequent. *Fibroma*, *myoma*, and *fibromyoma* and *lipoma* have been described. *Papilloma* of the mucous membrane occasionally form and they are probably the starting-point of primary carcinoma. Secondary carcinoma is the result of extension from uterine involvement. *Sarcoma* and *syncytioma malignum* are sometimes found.

Cysts of the Fallopian tubes are generally present, as hydrosalpinx, a consequence of obstruction. Small cysts attached to a somewhat long and narrow pedicle are known as *hydatids of Morgagni.*

EXTRA-UTERINE PREGNANCY

If there is any interference with the entrance of the impregnated ovum into the uterus an extrauterine development takes place. This may be within the ovary, between the tube

and ovary—*tubo-ovarian*—or, what is most common, within the tube— a *tubal* or *ectopic* pregnancy.

The chorionic villi are formed, deciduæ develop, and a placenta is evolved. At the same time there is commonly a decidua formation within the uterine cavity. As the embryo increases in size the walls of the tube become gradually thinner. By about the third month the tube generally ruptures. This may take place within the layers of the broad ligament, into the peritoneal cavity, or into the uterus. In any case there are severe symptoms of pain and shock and large internal hemorrhage occurs. It is very dangerous if the rupture has taken place at the placental site. Death may result from the loss of blood or from a peritonitis.

If the ovum has died the fetus may degenerate and become infiltrated with lime salts, forming a *lithopedion*.

If the impregnated ovum lodges somewhere on the peritoneum, we have an *abdominal pregnancy*. A similar condition is present at times when the ovum has escaped from a ruptured tube. In such instances the placenta usually remains within the tube. Peritonitis commonly ensues, the fetus perishes, and a lithopedion may form.

THE UTERUS

Congenital malformations are not infrequent and are the result of imperfect development of the Müllerian ducts. These ducts are two parallel tubes that normally unite in their long axis, forming in this way the uterus. There may be marked hypoplasia of the uterus and vagina, with very imperfect development of the tubes and ovaries. By failure of fusion of the ducts the uterus may contain two cavities, and if it extends downward divide the vagina into two canals.

Atresia or *stenosis* of the os uteri may be either congenital or the result of inflammatory conditions. On account of the obstruction the uterine cavity may become *dilated* by the retention of fluids. If by menstrual discharges, is known as *hematometra;* by seromucous secretion, *hydrometra;* if decomposition occurs and gas is formed it is then a *physometra;* when pus is present, is a *pyometra*.

Rupture of the uterus may result from the retention of fluid with gradual thinning and degeneration of its walls. It generally happens as an accident during pregnancy or labor. There may be some diseased condition, particularly malignant, of the muscle, or the wall may give on account of too great contraction of its fibers. If the tear does not extend all the way through the wall, it is an incomplete rupture; is complete whenever the serous covering is involved. The condition is associated with shock, and generally very severe and frequently fatal hemorrhage. If death does not result from the loss of blood, it usually follows from peritonitis. Sometimes the wound will cicatrize, the fetus degenerate and be discharged through fistulæ, and the patient recover.

In rupture the tear begins, as a rule, just above the cervix on the inside and extends in the direction of the fundus. If the uterus has been perforated by an instrument, the larger opening of the wound is on the outer surface, the opposite to what occurs in rupture.

Malpositions of the Uterus.—Normally the uterus is in a position of slight anteflexion and anteversion. The common displacements are either forward or backward, as the broad ligaments prevent lateral changes. In pathologic *anteflexion* the uterus is greatly flexed or bent, allowing the fundus to fall forward and downward. As a result the uterine cavity is obstructed and the menstrual fluid retained, giving rise to dysmenorrhea. In *anteversion* the fundus of the uterus falls forward and the cervix is displaced backward without a change in shape. In *retroflexion* the uterus is bent backward at an angle, the fundus falling downward and backward toward Douglas's pouch. *Retroversion* refers to a bending backward of the uterus without any change in the shape of the organ. Although they may occur separately, retroflexion and retroversion are generally associated. These deformities may be due to pressure from above, from the presence of new growths, from tight clothes, or to the presence and contraction of inflammatory adhesions. They may also be brought about by disease of the uterus itself.

The uterus may be elevated as a result of the presence of

tumors within the pelvis or of the contraction of adhesions dragging the organ upward. The opposite condition, *prolapse* of the uterus, or *procidentia*, is comparatively frequent. It is apparently due to a loss of tone in the structures supporting the organ, as in a torn perineum, or to an enlargement of the uterus. As it descends the vagina is slowly invaginated. According to the extent of the prolapse three degrees of severity may be considered. If the descent is slight and the uterus does not leave the pelvis, it is a *simple* prolapse; if the organ is not entirely out of the pelvis, it is a *partial* prolapse; if the uterus has descended to the vulva and discloses the vaginal walls, it is a *complete* prolapse or *procidentia*. In this latter the rectal and vesical walls are also dragged down, causing a *rectocele* and a *cystocele*. *Inversion* is a condition in which the uterus is more or less completely turned inside out. It occurs during labor, from large polyps or from localized pressure on the fundus. This condition is often accompanied by prolapse.

Stenosis of the cavity of the uterus may result from various inflammations or may be congenital. As a result of the blocking of the outlet *dilatation* of the uterus not infrequently occurs.

Circulatory Disturbances.—*Active hyperemia* is normally present during menstruation and pregnancy, and is similar to what takes place in pathologic conditions. The mucous membrane becomes much congested and swollen and there is a round-cell infiltration between the glands, which are somewhat increased in length. There is probably little or no desquamation of the surface epithelium. Serum is secreted and this may be hemorrhagic or purulent according to the diapedesis of erythrocytes or the emigration of leukocytes.

Passive hyperemia may be part of a general stasis, but is especially marked in severe malpositions or when neoplasms press upon the venous plexuses. The uterus is enlarged, dilated veins are seen on the outer surface, the mucosa is dark red, and the condition generally terminates in a chronic hyperplastic endometritis.

Hemorrhage may be normal, as in menstruation, or patho-

logic. The blood may be within the uterine cavity, in the uterine walls, or outside in the peritoneal cavity. When the menstrual period is lengthened and more blood than is normal is lost, it is known as *menorrhagia;* if the hemorrhage is between the menstrual periods, *metrorrhagia.* Normally the mucous membrane remains intact, but under certain pathologic conditions large masses of endometrium may be discharged; this is called *dysmenorrhea membranacea.*

In hemorrhage into the peritoneum the blood usually collects in Douglas's pouch. It may be derived from a ruptured tubal pregnancy, a hematosalpinx, or ruptured varicose veins of the broad ligament. The resulting hematoma may be large or small, and it may become absorbed or be encapsulated. Inflammation may occur with the formation of adhesions between the uterus and rectum. Occasionally the blood may escape by perforations into the rectum or vagina. Death may follow the loss of blood.

Atrophy occurs normally in old age, or as a consequence of the removal of the ovaries. The uterus becomes much smaller, dense, and pale, and the blood-vessels show an obliterative arteritis. The endometrium is also greatly reduced in thickness and the greater part of the glands is lost.

Following childbirth the uterus under normal conditions at first rapidly atrophies, then decreases more slowly. By the end of the fourth month it has usually regained its normal size. This process of involution consists essentially in a fatty atrophy of the muscular fibers, which decrease not only in size but also in number.

Hypertrophy may involve the entire uterus, as in the enlargement in pregnancy or in chronic congestion and inflammation. Local hypertrophy generally involves the cervix, which becomes much elongated and may present itself at the vulvar orifice.

Fatty degeneration other than the above is unusual, but has been found in typhoid fever, cholera, and in phosphorous poisoning.

Amyloid degeneration is rare; either the arteries or the muscle may be alone involved.

Inflammation of the uterus, if of the outer serous surface, is a *perimetritis;* of the muscular coat, *metritis;* of the lining mucous membrane, *endometritis.*

Perimetritis may result from puerperal infection, or be a part of a general or local peritonitis. In the acute form there may be a layer of pseudomembrane over the uterus and even involving neighboring structures. The process soon becomes chronic with the formation of adhesions. *Parametritis* is an inflammation of all the structures of the uterus accompanied by a cellulitis of the broad ligament and pelvic tissues. Usually occurs as a result of puerperal infection.

Metritis may be acute or chronic. The *acute* form generally occurs during the puerperium, but may be the result of gonorrheal infection. The uterus is much enlarged, congested, soft, and infiltrated with leukocytes. Occasionally small abscesses may form. The muscle fibers degenerate, thrombosis of the uterine sinuses and veins is quite common, and gangrene sometimes occurs.

Chronic metritis usually follows the acute form, or is the result of delayed involution of the uterus. There is a round-cell infiltration along the blood-vessels, the connective tissue increases and by contraction causes the muscle-fibers to atrophy. The uterus finally becomes small, pale, and dense. The entire organ is commonly involved, but occasionally the cervical portion is alone affected—it becomes enlarged, congested, and soft at first but afterward indurated.

Acute endometritis is usually the result of infection by pyogenic organisms or by the gonococcus. It may be found in the course of certain infectious diseases, as typhoid fever, cholera, scarlet fever, and diphtheria. The mucous membrane is very hyperemic and swollen, and there is quite extensive desquamation of the epithelial cells. Small hemorrhagic areas are seen, and there is a marked mucopurulent exudate. There are round-cell infiltration and necrosis of the epithelium; the formation of a pseudomembrane may occur. In gonorrhea the cervical portion is the usual seat, in other infections the fundus.

Chronic endometritis may follow the acute variety, or result

from general debility, local congestion and malnutrition, or from the irritation of tumors.

The mucous membrane is swollen, there is some round-cell infiltration and a more or less marked mucopurulent secretion. As the condition persists there is an increase in either the interstitial tissue or the uterine glands. In *endometritis glandularis* the increase in the size and number of the glands is the striking feature. The glandular hyperplasia may be so

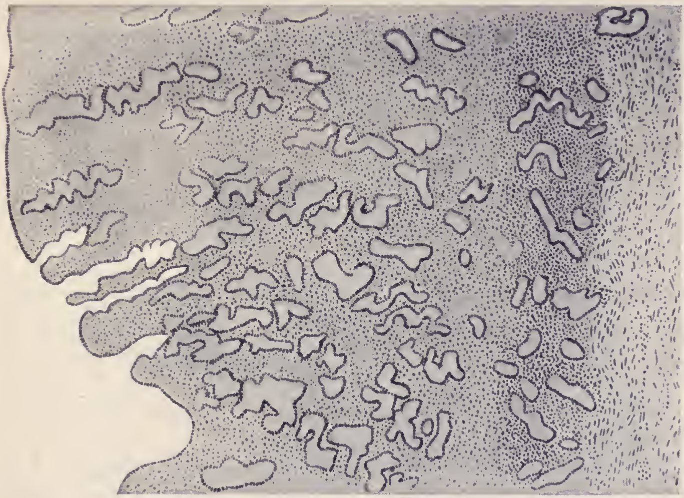

FIG. 177.—CHRONIC GLANDULAR ENDOMETRITIS. × 40 (Dürck). Uterine glands greatly proliferated, lengthened, and convoluted.

great as to closely resemble an adenoma. It is difficult to determine from the microscopical examination whether the lesion is a hyperplasia or chronic inflammation, or merely a phase of the menstrual changes of the endometrium. In *endometritis interstitialis* the glands are much fewer than normal, and there is a round-cell infiltration and hyperplasia of the interglandular connective tissue.

Atrophy may occur in late stages of chronic endometritis and the glands be displaced by connective tissue. In this process the openings of the acini, particularly of the Nabothian

glands of the cervix, may become obstructed and give rise to small retention cysts.

Chronic endometritis may give rise to chronic metritis or by extension involve the tubes

Ulceration or *erosion* of the cervix is very common, and results from endometritis and from lacerations. There is a destruction of the superficial epithelium with exposure of the deeper tissues. Occasionally there may be a rapid *phagedenic* ulceration with great destruction of tissue extending to the bladder and even to the rectum. Has been thought to be carcinomatous, but microscopic examinations have been negative.

Lacerations of the cervix result from childbirth; they may be simple, double, and multiple or stellate. They are very slow in healing and the exposed surfaces become covered by granulations. Fibrous connective tissue is usually formed, and the part may become very dense and hard.

Tuberculosis of the uterus is nearly always secondary to that of the tubes. The endometrium is usually affected and presents either a nodular or a diffuse infiltration. At times the endometrium may be completely transformed into a caseous mass.

Syphilis of the uterus is rare, but may occur as a chancre upon the cervix or as gummata.

Tumors.—*Fibroids.*—These tumors are the most common of those of the uterus. Although spoken of as fibroma, they nearly always contain a large amount of involuntary muscle, so the term *fibromyoma* is the more correct. They occur very frequently in negroes. They are classified according to their situation into: *mural*, *intramural*, or *interstitial*, when occurring within the muscular body of the uterus; *submucous*, when beneath the endometrium; and *subperitoneal*, when beneath the peritoneal covering. The tumors may be single or multiple, and their size varies from a pea to one weighing fifty pounds. The largest are the subperitoneal, as their growth is practically unlimited.

The density of the tumors depends upon the amount of fibrous tissue present. They are generally encapsulated.

The blood-supply is poor, so degenerations are common. These usually begin in the center of the tumor, and the most frequent form is calcification. If the tumor has been a pedunculated one, the pedicle may become twisted and necrosis set in. Fibromata may be associated with lipoma, myxoma, or sarcoma.

Fibroid tumors, although of the benign type, may give rise to severe symptoms on account of exerting pressure upon neighboring structures. The submucous type is often associated with hyperemia and hemorrhage from the endometrium or from a degenerated growth. Infection with necrosis and gangrene may take place. Labor may also be interfered with by the presence of such tumors.

Sarcoma of the uterus usually originates within the connective tissue between the muscle-fibers and about the vessels or occasionally from the muscle cells—*myoma sarcomatodes*. It may also arise within the submucous tissue. The myometrial sarcoma is generally spindle-cell in character; is grayish-white and soft; the endometrial is commonly round celled. *Angiosarcoma* is rare, and the so-called adenosarcoma is probably nothing more than an inclusion of the pre-existing endometrial glands.

A peculiar tumor occurring in early life is the edematous papillary sarcoma of the cervix. It is composed of a mass of soft, grayish, grape-like structures, that microscopically are made up of myxomatous round and spindle cells. There are also found epithelial tubules, areas of cartilage, and both smooth and striated muscle-fibers. Is quite malignant.

Papilloma appear on the cervix as rather small, cauliflower-like growths, composed of connective-tissue villi covered by many layers of squamous epithelium. Venereal warts are sometimes found upon the cervix.

Adenoma as such occur as polypoid projections from the mucous membrane, or as a glandular hyperplasia of the endometrium. They are benign.

Malignant adenoma, or *adenocarcinoma*, usually arises in the fundus of the uterus, upon the posterior wall. It is characterized by the tendency of the glands to invade the uterine

muscle and by the epithelium breaking through the basement membrane. Quite frequently the epithelium proliferates so rapidly that the acini become completely filled with cells, the glandular character is lost, and the tumor assumes a typical carcinomatous structure. Metastasis is unusual; the destruction is mainly local. The invasion and destruction of the muscle progresses until the bladder and the rectum may become involved (see Fig. 65).

Carcinoma is usually an adenocarcinoma and the progress is practically similar. There is rapid infiltration with extensive ulceration. The vaginal walls and the tissues in the neighborhood of the cervix become involved. The neighboring lymphatic nodes are frequently the seat of metastases.

Squamous epithelioma of the cervix is the commonest type of malignant tumor. In many cases it probably begins as a papilloma. There is soon developed a tendency of the cells to infiltrate the surrounding tissues and to grow superficially as a cauliflower mass. The growth extends downward, involving the vagina; extensive ulceration, accompanied at times by severe hemorrhage, occurs, and there is an extremely foul discharge. The tumor extends in all directions, and may perforate into the bladder or rectum or into the peritoneal cavity, giving rise to fatal peritonitis. In consequence of the loss of blood and absorption of harmful substances resulting from the breaking down of the tissues, there may develop a well-marked anemia and cachexia.

In old people squamous epithelioma may occur in the body of the uterus when metaplasia of the columnar epithelium has taken place.

Syncytioma malignum, or chorio-epithelioma, is a peculiar malignant tumor developing from embryonal tissue. The greater part of the cells are supposed to be derived from the syncytium. Is a rare form of growth (see p. 165).

Cysts of the uterus may result from a liquefaction necrosis of a fibromyoma, or from the obstruction of the Nabothian follicles. Dermoid cysts are occasionally found. Parasitic cysts due to the cysticercus and echinococcus have been described.

THE VAGINA

Malformations.—The vagina may be imperforate in its entire length or only partially. There may be a septum dividing the canal in two; such a condition is usually associated with a double uterus. Stenosis is seldom congenital; is generally secondary to some ulcerative condition.

When there has been a loss of support, as from a torn perineum, there may be a prolapse of the vagina, usually of the anterior wall. As the tissues relax the bladder is gradually involved; it is dragged downward and appears as a bulging of the vaginal wall—a *vaginal cystocele.* If the posterior wall prolapses and drags in the rectum, it is known as a *vaginal rectocele.*

Wounds may result from the introduction of foreign bodies, from coitus, or from injury during childbirth. If the injury or destruction to the part has been severe, *fistulæ* may be established between the vagina and neighboring structures. Communication between the bladder is known as a *vesico-vaginal fistula;* with the urethra, *urethrovaginal;* with the rectum, *rectovaginal.* Severe secondary inflammations may result from infection by urine or feces.

Inflammation of the vagina, *vaginitis* or *colpitis*, may be due to injury, as from hot douches, to the presence of foreign bodies, to the oxyuris, or to gonorrhea. In mild attacks there is a simple catarrhal inflammation, the mucous membrane becomes reddened, swollen, and covered by a slight alkaline mucopurulent secretion. In the gonorrheal form the reactions are more severe, the discharge is more purulent, and the cervix and urethra are generally involved. Occasionally when the inflammation is of a very high grade the mucosa may be exfoliated, almost as a cast of the vagina. A *pseudo-membrane* may be formed in the course of pneumonia, pyemia, and other infectious diseases. The mucous surface is covered by a dirty grayish pseudo-membrane that is eventually cast off, leaving quite extensive ulcerations. This may be followed by necrosis of the vaginal walls.

Chronic vaginitis or *leukorrhea* may follow acute attacks or

be the result of constitutional disturbances. Is commonly known as "the whites," on account of the presence of a thick, creamy exudate, acid in reaction. The mucosa is reddened and swollen, and resembles the condition seen in acute vaginitis. The discharge at times is thinner and contains less pus. Sometimes there may be marked thickening of the vaginal mucosa with very little discharge.

Tuberculosis of the vagina is secondary to similar disease of either the uterus—in which case it appears as rounded ulcers—or if of the vulva it is in the form of lupus.

Syphilis of the vagina is unusual. It may appear as a chancre, a mucous patch, or in the form of ulcers. Gummata may form and through regeneration give rise to distortion of the vagina as the scar-tissue heals.

Tumors.—*Fibromata* or *fibromyomata* are found in the submucous and muscular layers as either projecting nodules or as polyps. *Sarcomata* are rare. *Papillomata* are fairly common. *Carcinoma* is usually secondary to cancer of the cervix or of the rectum. When primary, is usually of the squamous epithelioma variety and cauliflower-like in its growth.

Cysts of the vagina are usually the result of obstructions of the follicles. They are generally small and may be single or multiple. Some of the larger cysts may develop from remains of the Wolffian or Müllerian ducts. May also be the result of lymphangiectasis.

THE VULVA

Wounds are particularly common as a result of childbirth. They generally occur as lacerations of the posterior fourchette and may extend not only into the perineum but into the rectum. If the damage has been very severe, extensive necrosis and even gangrene may follow. Severe hemorrhage is also not uncommon, forming a hematoma within the labia. If comparatively mild infection takes place, abscesses may form.

Hyperemia may be due to acute inflammatory conditions or occur as a result of local irritation, as from the oxyuris. Is accompanied by increased exudation. Passive hyperemia may

be a part of a general venous stasis or the result of some local obstruction to the outflow of blood.

Inflammation of the vulva may be the result of many conditions: uncleanliness, gonorrhea, or injuries. The parts become reddened, swollen, edematous, and are accompanied by a marked exudation that may be mucoid, serous, or purulent, or any combination of the three. Pseudo-membrane may form and gangrene also may occur. Abscesses may be due to infection or to extension.

Noma pudendi is a form of gangrene that occurs spontaneously in debilitated children; it resembles noma of the face. Is very rare.

Tuberculosis, in the form of lupus, is sometimes encountered. Occurs as irregular ulcers, with necrotic bases and elevated edges.

Syphilis, usually in the form of a chancre, occurs on the vulva. Ulcers of various forms may be present, and mucous patches are very common.

Chancroid is quite frequent; is accompanied by extensive ulceration and, at times, inguinal buboes.

Elephantiasis may involve one or both labia, and cause a tremendous increase in the size of the part.

Tumors.—*Fibroma* and *fibromyoma* are occasionally found projecting from a labium or the clitoris, as polypoid tumors. *Lipoma*, as a polyp from the labium majus, is not uncommon. *Sarcoma* is rare. The *caruncle* is a small papillary growth projecting from the urethra, is very vascular, and extremely sensitive. *Papillomata* are quite common, and occur as hard, flat, or projecting masses; are present in syphilis. *Cancer* is rare, but may arise from the skin, the labium majus, or from the glands of Bartholin. Usually occurs as a squamous epithelioma, which commonly undergoes marked degeneration and ulceration. It extends in all directions, and secondarily affects the inguinal glands.

DISEASES OF THE MAMMARY GLAND

Malformations.—As an associated condition with imperfect development of the chest-walls one or both glands may be

absent. They may be hypoplastic, when there is also an incomplete development of the sexual organs. A breast may be normal in other respects, but be lacking a nipple, or there may be several nipples. Supernumerary mammæ—*polymastia*—may be present in both sexes, usually on the anterior surface of the chest and abdomen. They may occur on the back or thigh, and occasionally may functionate, although they are usually ill developed and lack a nipple.

Circulatory Disturbances.—*Hyperemia* is present during menstruation, during pregnancy, and at the beginning of lactation. The gland will be reddened, swollen, and sometimes painful. This congestion may also be brought about by some diseased condition of the uterus, the relationship of these two organs being very close.

Hemorrhage is due to some injury of the gland. The bleeding may take place within the connective tissue, into the glandular structures, or deeper down, behind the gland upon the muscle. The blood may escape from the nipple, it may be absorbed, or it may become encapsulated by a wall of fibrous tissue and form a hematoma. Hemorrhage may also be the result of bleeding from the ulcerated surfaces of new growths.

Inflammation of the mammæ, or *mastitis*, may rarely be due to injury, but it is most commonly the result of infection occuring during the puerperium. The micro-organisms most frequently gain entrance through fissures of the nipple during suckling. Infection directly into the milk-ducts is not common. Mastitis may result from the extension of inflammations of neighboring structures, as caries of a rib, erysipelas of the skin, or in puerperal infection the micro-organisms may have been brought to the gland through the blood-vessels. The disease may be diffuse or involve a portion only of the gland, the latter being the more common. In the diffuse form the inflammation may extend to neighboring structures, setting up a *paramastitis*. In the circumscribed variety there is abscess formation, which may be single or multiple. The pus may escape into the milk-ducts and out through the nipple; it may be interstitial or rupture externally, in the latter case frequently causing a fistula. If the pus burrow into the deeper

tissues, it may perforate into the pleural cavity and cause a fatal empyema. Occasionally the pus may be encapsulated, inspissated, and calcified. Sometimes a condition of the mammæ similar to that of chronic interstitial inflammation of the organs occurs. The glands are firm and hard, due to the connective-tissue formation, and small cystic dilatations of obstructed milk-ducts may be present.

Tuberculosis of the mammary glands is rare, except as a secondary involvement in tuberculosis of the axillary nodes or other tissues. The tubercle bacilli are probably carried by the blood. Tubercles are formed which undergo caseation, and the contents escape into the acini. In this way great numbers of the bacilli can gain entrance into the milk.

Syphilis of the mammæ is very rare, but has been seen as gummata, which in healing form a dense, stellate scar.

Atrophy of the glands occurs after the menopause or when the ovaries have been removed.

Hypertrophy at the time of puberty may continue beyond the normal limits and cause an enormous development of both the glandular and connective-tissue elements of either or both breasts. If lactation takes place, the amount of milk secreted may be very great. The gland may be much enlarged, on account of a diffuse fatty infiltration or *lipomatosis*.

Tumors.—*Sarcoma* is rather infrequent, is usually of the round-cell variety, and may be diffuse or in circumscribed nodules. One gland alone is generally involved. In the diffuse form the mamma rapidly enlarges, the growth infiltrates in all directions, the skin soon becomes firmly attached and may ulcerate. The structure of the tumor differs in different parts. It may be quite cystic on account of obstruction to the milk-ducts; part may be myxomatous or resemble connective-tissue. The sarcoma cells may extend into the cystic dilatations as polypoid projections—*intracanalicular sarcoma*.

Occasionally the tumors may be circumscribed. They most commonly originate within the adventitia of the milk-ducts and nipple, but may arise from any part of the connective-tissue of the gland. These tumors give metastasis by

means of the blood, but they are much less malignant than the carcinomata.

Fibroma as a pure connective-tissue tumor is unusual. It is commonly found in connection with a hyperplasia of the glandular structures.

Adenoma in a typical form is rare, is generally associated with an overgrowth of connective-tissue, and is called either *adenofibroma* or *fibro-adenoma.* According to the relation of the glandular and fibrous elements these tumors can be classified into three divisions:

Intercanalicular fibro-adenoma, in which the tumor is chiefly fibrous in structure, with the ducts and acini irregularly distributed through it.

"*Pericanalicular fibro-adenoma*, in which the fibrous tissue makes distinct concentric investments of the ducts and groups of acini.

"*Intracanalicular fibro-adenoma*, in which polypoid or papillary growths extend into the ducts."

These tumors are more or less completely encapsulated, and although of the benign type, they not infrequently take on a carcinomatous growth.

Carcinoma is an extremely common tumor of the mammary gland in women between the ages of forty and fifty. About 2 per cent. of cases occur in males. The growth usually involves one breast only, and that the right more frequently than the left. It develops either from the tubules or the acini of the glands, and may start as a carcinoma or result from a malignant degeneration of a fibro-adenoma. When the growth begins in the acini, it resembles quite closely the ordinary racemose character of the gland—is alveolar in form. If it is of the tubular type, there are long tubular collections of cells.

Although at first the growth may quite closely resemble a simple adenoma, proliferative changes soon occur in the epithelium. The cells, instead of forming a single layer, increase in number and lose their resemblance to the normal structure. These new-formed cells may completely fill the acini, or they

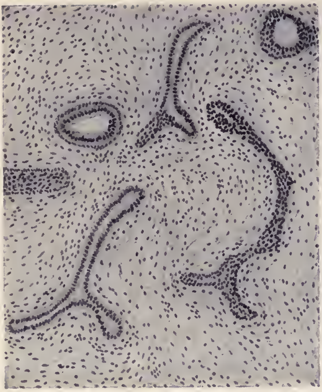

FIG. 178.

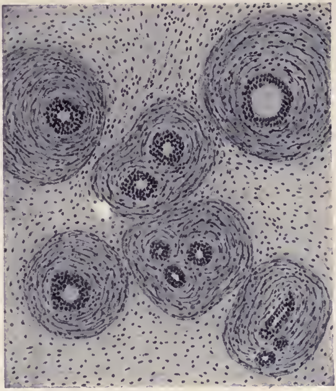

FIG. 179.

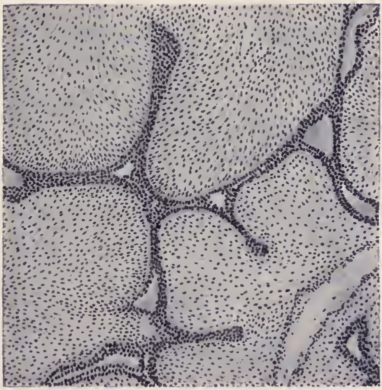

FIG. 180.

FIG. 178.—Intercanalicular adeno-fibroma of mamma. The fibro-connective tissue bears no definite relation to the glandular canals. Fig. 179.—Pericanalicular adeno-fibroma of mamma. The fibro-connective tissue shows a peculiar concentric relation to the glandular canals. Fig. 180.—Intracanalicular adeno-fibroma of mamma. Papillary connective-tissue growths project into the glandular canals (McFarland).

may be found within the surrounding tissue as a result of destruction of the basement membrane.

According to the relationship between stroma and parenchyma mammary carcinoma may be divided into three classes:

Carcinoma simplex, in which there is, relatively speaking, an equal amount of connective-tissue and epithelial cells. Is less malignant than the medullary, but more so than the scirrhous.

Encephaloid or medullary carcinoma, which is very rich in cells and poor in stroma, is soft, contains much "cancer juice," and hemorrhages are not uncommon. It grows rapidly, soon ulcerates, and is rapidly fatal.

Scirrhous carcinoma is characterized by a great preponderance of connective tissue, is hard, is slow in growth, does not tend to give metastases, and is slowly fatal. In this form there is frequently a retraction of the nipple.

The so-called *colloid* carcinoma of the breast is generally one in which a myxomatous degeneration of the connective tissue has given rise to the appearance.

Extension of carcinoma may take place directly to the skin or, by penetrating deeply, enter the chest-walls and pleuræ. Metastasis is common, takes place early, and may be very extensive, the axillary nodes being first involved. Secondary growths may also occur in distant parts of the body.

Paget's disease begins as a chronic eczema of the nipple and adjacent skin. It may have existed for ten or fifteen years with more or less complete destruction of the nipple, and then take on a carcinomatous change.

Cysts are quite commonly found, particularly in new growths in which there has been an attempt at secretion without any outlet. Small milk-cysts may result from obstruction to the ducts. The contents of the cysts may be milky, or, through absorption of the liquid portion, become thick and caseous. In some cases there are polypoid outgrowths of connective tissue and epithelium from the walls of the cysts.

CHAPTER XXIV

DISEASES OF THE MOTOR SYSTEM

BONES

Circulatory Disturbances.—*Hyperemia* is usually associated with inflammatory disturbances of adjacent tissues. The periosteum is reddened and swollen, and the marrow is bluish-red in color.

Thrombosis may occur in the nutrient blood-vessels as a result of fracture or disease, but seldom causes any disturbances on account of the rich anastomoses. *Embolism* may occur, but seldom causes trouble.

Hemorrhage takes place as a result of injury to the periosteum or the bone itself, as in fracture. Is generally soon absorbed, but if it becomes infected, suppuration may follow. Necrosis may at times be caused by the blood dissecting the periosteum away from the bone.

Rachitis.—*Rickets* is a constitutional disorder in which there are nutritional disturbances involving, to a greater or lesser extent, all the bones of the skeleton. The long bones become shortened, thickened, and twisted, and there is a lack of calcium salts, proper ossification not taking place. It makes its appearance most frequently in the first or second years of life, but may be delayed until several years later. The cause is not known, but it evidently depends upon poor hygiene and malnutrition, consequently it is more common among the poorer classes.

The head has a peculiar square shape and is large in proportion to the body. In infants the anterior fontanel may persist for three or four years, and the bones of the skull may contain localized areas in which there is a lack of mineral salts—*craniotabes*. The chest is usually prominent, coming to a distinct angle—"pigeon-breast"—and the anterior ends

of the ribs at the junction with the cartilage are distinctly enlarged, forming the *rachitic rosary*. If the disease is severe, there may be involvement of the spinal column. If the curvature is forward, *lordosis;* if backward, *kyphosis;* sideways, *scoliosis*. These curvatures may occur in combination. The pelvis may show changes that have a direct influence upon childbirth; it is distinctly flattened. The anteroposterior diameter is decreased, while the transverse is increased. The tibiæ and fibulæ are usually much curved outwardly, the femur anteriorly. The deformities are due to the fact that the bones, lacking lime salts, are not stiff enough to resist the pull of the muscles nor outside pressure. The lesions are most marked at the extremities of the long bones. Microscopically there is seen at the extremities an irregular bone-formation with a deficiency of lime salts in many areas, while neighboring portions will show ossification. The normal laminated appearance is absent.

The marrow is of the red variety, similar to that in the fetus, being rich in cells. The increase in size of the heads of the long bones is due to an increase of the cartilage cells and enlarged marrow-spaces. Associated with the lesions of the bones are gastro-intestinal disorders and fibrous hyperplasia in both spleen and liver. There is a decrease in the erythrocytes and an increase in the leukocytes.

Osteomalacia is a condition of softening and flexibility of the fully formed bone following absorption of the bone salts. It is most common in women of the poorer classes, and frequently appears in connection with pregnancy. It is more common in certain regions—along the Rhine and in central Germany—than elsewhere. As a result of the flexibility of the bones, fractures are very common and all varieties of deformities may appear. The pelvis is often the seat of a typical deformity. As a result of the pressure of the spinal column from above and from the femurs below, the pubes are pushed upward and forward like a beak, the sides of the pelvis inward, and the iliac crests outward. From above, the opening in such a pelvis is triangular. Microscopically it is seen that the loss of bone salts takes place first at the periphery and

extends toward the center. The laminated condition remains unchanged until late in the disease. The marrow is congested and red, the fat absorbed, and there is an extensive collection of small, round cells. The marrow may become gelatinous in appearance. Where the bones are much bent or there has been a fracture, the regular histologic structure is not retained. The bones are soft and easily broken or cut. Cachexia appears eventually, and the patient usually dies from exhaustion following repeated fractures or from some intercurrent disease.

Atrophy of the bones occurs constantly, but regeneration continues also, except when the atrophy is due to senile changes. In various conditions the destruction is too rapid and actual atrophy takes place—either general or local. Local atrophy is usually the result of pressure causing obstruction of the periosteal blood-vessels, thus interfering with the nutrition of the bone. This is not really an atrophy but a rarefying osteitis. When the bones become very brittle as a result of atrophy, the condition is known as *fragilitas ossium.*

Hypertrophy may be general or local, the latter being due to increased work brought upon certain areas of muscular attachment. General enlargement seems to be due to various nerve disturbances, and is frequently associated with lesions of the pituitary body, as in a akromegaly.

Inflammation may involve the covering of the bone—*periostitis*—the bone itself—*ostitis*—or the marrow—*osteomyelitis*. It is due to traumatism and infection.

Periostitis may be acute or chronic. In the *simple* or *acute* form the periosteum becomes swollen, hyperemic, and infiltrated with blood. The process may stop there, but if infection has taken place, pus collects in the inner layers of the periosteum, and between it and the bone. This accumulation of pus may dissect the membrane from the bone and form a subperiosteal abscess. The pus may be absorbed, become dry and cheesy or burst through the periosteum and cause abscesses in the adjacent tissues. In such a case the nutrition of the bone is interfered with, and the osseous tissue begins to undergo destruction—*necrosis*. Large portions may separate and be

discharged as *sequestra* through a superficial opening. The process may extend into and involve the marrow cavity, and death may result from septicemia or pyemia. The so-called *malignant periostitis* is merely a very severe purulent periostitis of considerable extent, and accompanied by marked destruction of the bone.

Chronic periostitis may have originated as such, or it may have followed an acute form. It may be *fibrous*, in which the periosteum becomes very greatly thickened and adheres very closely to the bone. *Ossifying periostitis* is a condition in which there is the formation of loose bony tissue from the inner layers of the periosteum. It is found in pregnancy, in tumors, and in syphilis and tuberculosis of the bones.

The bony masses are called *osteophytes* and at first have a loose spongy character and are not firmly attached to the old bone. Later, however, layers of dense compact bone are deposited within the medullary spaces until the entire mass may become as compact or even more so than the normal bone. At the same time they become firmly attached.

Osteitis and osteomyelitis have to be considered together, as the two conditions do not exist separately. This condition results from infection, either by micro-organisms from the blood, from local infections, or from a pre-existing periostitis. The inflammation generally starts in the medullary cavity of the long bones, the marrow of which is much congested at first and dark red in color. Later there is a cellular infiltration, and finally suppuration occurs, the pus being localized or in streaks. The surrounding bone becomes involved, and more or less extensive necrosis follows. The periosteum becomes inflamed, and the suppuration may extend to and involve the epiphyses. The necrotic portion may remain as a sequestrum, being surrounded by a layer of normal bone. As long as the sequestrum remains, healing will not take place, but when it is removed, either entire or by absorption, new bone is formed and there is a return to nearly the normal. When the condition terminates fatally, it is generally due to pyemia.

Chronic osteomyelitis generally is a condition following the acute form as a result of a retained sequestrum. The changes

in this disease are more marked in the bone than in the marrow. There are two varieties of the chronic form: *osteoporosis,* in which absorption takes place with an increase in the size of the Haversian spaces. The bone becomes more spongy, and the enlarged spaces become filled with marrow; *osteosclerosis,* in which there is an increased formation of bone, particularly beneath the periosteum, but also within the marrow cavity. The subperiosteal deposit may be very dense and possess an ivory-like eburnation.

Rarefying osteitis consists of the formation within the marrow spaces, Haversian canals, or beneath the periosteum of a new, very cellular and vascular tissue, resembling granulation of young marrow tissue. This causes an absorption of the basement substance of the bone.

Necrosis refers to the destruction of large portions of bone, as a result of interference with the blood-supply or from the extension of disease from the periosteum or neighboring bone.

The dead piece remains as a *sequestrum;* part having been absorbed, the rest remains in a cavity surrounded by granulation tissue and pus. It acts as a foreign body, and constantly keeps up a suppurative reaction in the adjacent structures. A fistulous opening or *cloaca,* communicating with the exterior, generally forms, and the pus continues to discharge through it. This may continue for years if the sequestrum is so large that it cannot pass through the opening. When it does escape or become absorbed, healing takes place. *Phosphorous necrosis* of the maxillæ is frequently observed in those who are employed in the manufacture of phosphorous matches. The process begins as a thickening of the periosteum, with suppuration, caries, and necrosis, which may be very widespread and destructive. The condition is favored by the presence of carious teeth.

Tuberculosis of the bones is most frequent in childhood and may begin during uterine life. The epiphyses of the long bones are most commonly involved, then the spinal column, the wrist- and the ankle-joints. The infection may be hematogenous from tuberculosis of other organs, or it may result from direct extension by contiguity. The disease may occur in a miliary

form within the bone-marrow, or as a localized condition of the periosteum. The process extends more rapidly in the spongy bone and frequently involves the joints.

In the marrow cavities of the bone tubercles appear as small grayish areas surrounded by a zone of active hyperemia. These extend through the Haversian canals, involving compact as well as spongy layers. These areas undergo caseation and are accompanied by caries of the bones. The degenerated masses may so obstruct the blood-supply as to cause necrosis. As the bone is destroyed, broken-down masses are formed, and these may escape into the surrounding tissue, giving rise to a cold abscess. There is little inflammatory reaction; the degenerated tissue follows along the lines of least resistance, along muscle-sheaths, and may finally be evacuated at some distance from the seat of the disease. This is particularly common in Pott's disease, tubercular caries of the spine. Occasionally encapsulation and absorption take place, but this is unusual. The periosteum surrounding the degenerated area may undergo a marked new bone-formation.

Very extensive deformities may ensue in this disease, either as a result of destruction of the bone or from the formation of osteophytes.

In long-continued tubercular degeneration of the bone, extensive amyloid changes in the internal organs are common.

Syphilis of the bones may be either hereditary or acquired.

In congenital syphilis the chief bony lesion occurs between the epiphysis and the diaphysis. The zone of calcification is broad, uneven and white or reddish-white in color. The cartilage at this point is much thickened, and the calcified portions project irregularly into the marrow cavity. As the condition progresses the cartilage may become almost gelatinous, and finally there may form a distinct, irregular, yellowish line of granulation tissue separating the diaphysis and the cartilage. This change is usually most advanced in the lower end of the femur, then in the lower ends of the leg bones and of the forearm, then in the upper ends of the tibia, femur, and fibula. This is one of the characteristic signs of congenital syphilis.

Acquired syphilis generally involves the periosteum and occurs usually in the tertiary stage. It may appear as a periostitis of the skull, tibia, ulna, etc., with thickening due to hyperplasia. This may become gummatous, set up a superficial erosion and necrosis of adjacent bones, with quite extensive loss of tissue. This is not infrequent in the skull.

Leprosy generally begins in the marrow in the form of nodules, and sets up an osteomyelitis. In one form, *lepra mutilans*, there may be marked destruction and absorption of the phalanges.

Actinomycosis gives rise to an osteomyelitis with more or less caries and necrosis.

Tumors.—The periosteum may be the seat of a *fibroma*, a *myxoma*, or a *lipoma*. *Chondromata* also develop from the periosteum, are most common on the extremities, and are generally multiple. The *osteomata* are tumors formed of bone.

Sarcoma is the most frequent and the most important bone tumor, being also the only primary malignant growth. Any of the various forms may occur, the spindle-cell and the giant-cell being the most common, but round-cell, pigmented, and angiosarcoma are occasionally seen. The tumor may originate from the periosteum, the bone-marrow, or the bone. The giant-cell sarcoma, or epulis, is found upon the lower jaw, is usually only slightly malignant; may last for years and not give metastases. When the growth originates within the medulla, myeloid sarcoma, the bone gradually becomes much thinned and may break, allowing the tumor-cells to escape. An *osteoid* sarcoma is one generally arising from the periosteum at the ends of the long bones, and is characterized by the formation within it of irregular masses of bone.

Secondary infection may give rise to a general sarcomatosis of the bony structures.

Myeloma is the name given to a group of tumors that although resembling the sarcoma histologically, are derived from the special cells of the bone marrow and not from the periosteum. They are usually multiple and appear as grayish or reddish masses in the spongy bone. Microscopically there are three varieties of tumor according to the type of cell that

predominates. Those composed of myelocytes; of red cells; and of plasma cells.

Chloroma is a form of sarcoma that is green or yellow in color, and is usually found in parts of the skull.

Carcinoma probably never occurs except as a secondary involvement, particularly in cases of carcinoma of the breast, thyroid gland, and prostate.

Fractures.—A fracture is a solution in the continuity of a bone, and is usually due to traumatism or to muscular contraction. The break may occur in any direction in the bone —transverse, oblique, or parallel to the long axis, or any modification. If the break is not complete of all fibers, it is known as a *green-stick* fracture; this is common in children. If there are several fragments it is called a *comminuted fracture.* If an opening to the surface is made, it is a *compound fracture.*

When a bone is broken, reparative processes take place and the bone is regenerated. After the fracture there is an extravasation of blood between the fragments. Proliferation of the cells of the periosteum occur, and calcareous matter is deposited, forming cartilage, or *callus.* This is slowly converted into bony tissue. At first there is an excess of it, but all except that immediately surrounding the fracture is absorbed. The callus is derived from the periosteum and from the medullary cavity. At the time of its formation new blood-vessels appear to assist in the nutrition. More or less deformity may accompany the process of repair, according to whether or not the broken fragments were carefully approximated.

DISEASES OF THE JOINTS

Luxation is a condition in which the articulating surfaces are disturbed in their relations. It is due to traumatism, and when it occurs, there is generally a rupture of some of the ligaments with laceration of the adjacent soft parts. If the surfaces are restored to their normal position, inflammatory reaction takes place, the capsule and the ligaments heal, and a normal condition supervenes. If restoration has been incomplete or only partial, absorption of the end of the bone occurs, the periosteum undergoes calcification, and a new joint may

be formed. Fibrous tissue, cartilage, or bone may, however, form, and bind the joint so closely that no motion is preserved; this condition is called *ankylosis.*

Hyperemia of the joints is found after injuries, in mild inflammations, and in rheumatic conditions. The synovial membranes are mainly affected. They are pinkish, swollen, and the synovial fluid is both increased in amount and more watery than normal.

Hemorrhage generally follows an injury, but may occur in inflammations and in the course of hemorrhagic diseases. It is called *hemarthrosis.* If infection does not occur, absorption slowly takes place, leaving the tissues considerably pigmented.

Arthritis, or inflammation of a joint, may be due to an injury or to a hematogenous infection in certain diseases, as scarlet fever, pyemia, or gonorrhea. The synovial membranes are chiefly involved, the cartilages less so and secondarily. If all the structures of the joints are involved, it is a *panarthritis.* The exudation into the joint may be serous, fibrinous, or purulent, and the after-results depend mainly upon which variety of arthritis existed. If *serous*, the fluid is generally soon absorbed and the joint returns to a normal condition. If, however, there is a *serofibrinous* exudation, the process will probably continue longer and adhesions form within the joint. The most serious variety is the *purulent.* The entire joint is frequently attacked, the synovial membrane swollen and hyperemic, and the surface covered by pus-cells and fibrin. The joint contains a greater or less amount of pus, and the articulating cartilages may be eroded and even necrotic, with involvement of the neighboring bone.

Any of the above varieties may become chronic, and in the serous form a *hydrarthrosis*, or collection of fluid in the joint, may be present. In the purulent variety, as a result of the destruction of cartilage or bone, the joint may lose all power of motion—ankylosis—from the formation of fibrous and bony adhesions.

Acute articular rheumatism is a condition in which one or more joints are acutely inflamed and painful. This proc-

ess is generally considered to be the result of infection; staphylococci, gonococci, and other organisms have been recovered from the affected joints. The joints are swollen, red, and painful, and the surfaces are covered more or less by masses of fibrin, some of which may be suspended in the exudate. There are seldom many leukocytes present. As a result of the inflammation, either fibrous or bony ankylosis generally occurs, with more or less subsequent deformity.

Arthritis deformans, or **rheumatoid arthritis,** is a chronic process occurring, as a rule, in people past middle life. There is a proliferation of cartilage cells, and finally softening, with ulceration of the superficial cells. This gradually extends down to the bone, the surface of which frequently shows some absorption. At the edge of the joint exostoses (abnormal bony outgrowth) may form. The ligaments become contracted and fibrous, and ankylosis occurs. As a result of the destruction of bone and formation of connective tissue, all varieties of subluxations (partial dislocation) and deformities occur.

The joints most commonly involved are those of the hip and knee, metacarpo-phalangeal articulations of the hand, and the corresponding ones of the feet.

Senile arthritis resembles very closely the former variety, except that it is more widespread, involving the hip, shoulder, and elbow, and occurs in old people.

Neuropathic arthritis occurs in spinal diseases, particularly posterior sclerosis, syringomyelia, and transverse myelitis. The joints of the lower extremities are more commonly involved. The lesions closely resemble those of arthritis deformans, but there is seldom much pain.

Arthritis uratica, or **gout,** is a condition in which there are deposits of urates within the joints and the adjacent connective tissues. It generally affects the smaller joints of the hands and feet, particularly the metatarso-phalangeal articulation of the great toe. The joint becomes red, swollen, and very painful; there is a serous effusion into it, and the salts are precipitated from this fluid. These substances may form quite large, chalky deposits. After repeated attacks chronic changes may occur within the joint, such as softening

and erosions of the cartilage, hyperplasia of the periosteum, with some ossification. Besides the local conditions, there are constitutional disturbances and also widespread tissue changes, particularly atheroma of the blood-vessels.

Tuberculosis of the joints is most common in childhood, and may be primary or secondary. It occurs most frequently in the hip, knee, and spine, although any joint may be attacked. In the primary form the synovial membranes are first involved. The secondary variety generally results from extension from tuberculosis of the bone.

In the synovial membrane are found extensive soft granulations in which are seen small yellowish or gray tubercles. Caseous degeneration appears early, as a rule, and the joint may be filled with broken-down tissue forming a cold abscess. When the process has extended from the bone, there is marked destruction of tissue around as well as within the joint. The abscess contents may burrow, and emptying upon the surface form a sinus.

Death may result from associated amyloid disease or exhaustion.

If the process subsides, the joint is usually ankylosed in an abnormal position.

Syphilis of the joints is found in children as a congenital lesion. There are thickenings of the ligaments, ulceration of the cartilages, and a purulent exudation. Occasionally gummata may be present. In adults, as a result of acquired syphilis, there may be a serous or sero-fibrinous inflammation of the joint. Gummata sometimes occur, and as a result of degeneration with fibrous formation may cause lesions similar to arthritis deformans.

Tumors.—The synovial fringes may show small lipomata and fibromata. These may become separated and lie free within the joint, the so-called "rice bodies," which are small structures originating from the villi of the synovial membrane; are generally quite numerous, thirty or forty being found at times. The joints may be secondarily involved by new-growths in adjacent tissues.

DISEASES OF THE TENDONS AND BURSÆ

Tenosynovitis refers to an inflammation of the sheath of a tendon and may be acute or chronic, or serous, fibrinous, or purulent, or any combination, according to the exudate. The purulent is usually the result of a secondary infection.

Bursitis, inflammation of the bursa, is usually found in the prepatellar bursa as a result of chronic irritation, and is accompanied by effusion.

Tuberculosis may involve either of the above structures secondarily to disease of the bones and joints.

DISEASES OF THE VOLUNTARY MUSCLES

Circulatory Disturbances.—*Anemia* may be part of a general condition or the result of local interference. Degenerations of the muscle occur if the anemia has been sufficiently severe or long continued.

Hyperemia occurs during exercise and in inflammatory processes.

Hemorrhage results from injuries or from the rupture of a blood-vessel that is either diseased or in which the blood-pressure has been too great.

Degenerations.—*Necrosis* of muscle-fibers may follow injuries, burns, and various local causes; the tissue becoming blackish in color and disappearing.

Cloudy swelling is found in infectious and toxic conditions in general and in the neighborhood of inflammatory changes and tumors. The sarcoplasm becomes very granular and the striations disappear. Fatty degeneration frequently follows.

Fatty metamorphosis follows the cloudy swelling when the original cause has been very harmful, as in phosphorous and arsenic poisoning. The muscles are flabby and yellowish in color. The fibers lose their striations and become filled with fat-drops.

Fatty infiltration consists of the deposit of fat between the muscle-fibers. It is most typical in pseudohypertrophic muscular atrophy, but may be present to some extent in obesity.

Amyloid degeneration is rare in voluntary muscles, but occurs occasionally in the non-striated.

Calcification occurs in the form of ossifying myositis.

Hyaline Degeneration.—In this the muscle-fibers become granular and cloudy, and the transverse striations are obscured. The hyaline change appears in streaks, the fibers having become transformed into a homogeneous mass within the sarcolemma. The fibers break in two, and rupture of the muscle may occur. The degeneration is found in the course of infectious conditions, as typhoid fever and smallpox. It is found usually in the rectus abdominis, in the long muscles of the thigh, in the diaphragm, and in the heart.

Atrophy.—Simple atrophy is usually either senile or the result of inaction. The fibers become smaller, and there is usually some hyperplasia of the connective tissue. *Brown atrophy* is quite common as a senile change. In it brown pigment particles are deposited in the muscle-fibers near the nuclei, and impart a brown color to the tissue.

Progressive muscular atrophy usually involves the muscles of the hands, arms, and shoulders, but may attack those of the diaphragm and back. The muscles are pale and flabby, and show various degenerations, such as transverse division, longitudinal separation, coagulation necrosis, and vacuolation. At the same time there is a connective-tissue hyperplasia.

Pseudohypertrophic muscular atrophy commonly makes its appearance in the muscles of the calf, thigh, and upper extremities. The muscles are much larger than normal, but are soft and flabby. Microscopically there is seen a great hypertrophy of the intermuscular connective tissue, with fatty infiltration and atrophy of the fibers.

Many of the muscular atrophies depend upon various obscure nerve lesions, as such changes are found in syringomyelia; acute anterior poliomyelitis; lateral scleroses; in degeneration of the peripheral nerves; in diseases of the anterior nerve-roots; in diseases of the pons, and possibly of the nerve-endings.

Inflammation or **myositis** is generally the result of in-

flammatory changes in adjacent tissues. It may be acute or chronic, local or disseminated.

The process is usually not severe; the muscle is swollen, reddened, and there is a slight exudation, as well as a round-cell infiltration. Some of the fibers may degenerate.

Hemorrhagic myositis is characterized by marked hemorrhagic infiltration into the muscle. It may follow extension from gangrenous processes near by.

Purulent myositis is characterized by local or disseminated abscess formations, with necroses and breaking-down of the muscle-fibers. It is due to infection by micro-organisms as a result of traumatism through conveyance by the blood or lymphatics or to infectious emboli. In the healing, masses of connective tissue may form and occasion more or less severe deformities, due to shortening. Sometimes an abscess may become encapsulated and calcified.

Acute disseminated polymyositis is a condition in which many muscles are simultaneously affected. It is of infectious origin. There is round-cell infiltration between the fibers, many of which show degenerative changes.

Chronic myositis may be a slow process, found in tuberculosis and actinomycosis, in which there is long-continued suppuration without fibrosis. The ordinary form is the *myositis fibrosa*, in which there is a slow increase in the amount of connective tissue with degeneration and atrophy of the muscle-fibers. It follows acute myositis and sometimes after certain nerve-lesions.

Myositis ossificans is a chronic inflammatory condition in which there is actual bone-formation within the intermuscular connective tissue, in fascia, and tendons. It is found in the deltoid, pectoral, and adductor muscles, and appears to be the result of long-continued and repeated slight injuries.

Myositis ossificans progressiva is a peculiar condition beginning in the muscles of the back of the neck. The ossifying process gradually extends to other muscles of the trunk. The deposit of bone may become very great and cause marked interference with muscular contraction.

Tuberculosis of the muscle is commonly secondary to le-

sions in adjacent tissue, and appears either in the form of caseous degeneration, cold abscess, or of fibrous formation. Hematogenic infection is uncommon in general miliary tuberculosis, but may occur.

Syphilis is rare, but may be found in the form of gummata, or as a diffuse hyperplasia of the muscular septa, with atrophy of the muscle-fibers. The muscles usually involved are the biceps, masseter, tongue, and back.

Glanders and **actinomycosis** may involve the muscles by extension.

Tumors, as a rule, originate within the intermuscular connective tissue and may be any one of that type—lipoma, fibroma, etc. The *sarcoma* is not infrequent in any of its combinations, and may be spindle- or round-celled in type. *Carcinoma* is always secondary, and is found in the neighborhood of similar growths in the mammæ, stomach, skin, etc., as a diffuse infiltration.

Parasites are not uncommon, the most frequent being the *Trichina spiralis*, the *Cysticercus cellulosæ*, and the *Tænia echinococcus*.

CHAPTER XXV

THE DUCTLESS GLANDS

THE THYROID

Malformation.—It may be congenitally absent, variations in size are common, and small accessory glands may occur. Total absence is usually associated with cretinism or idiocy.

Atrophy takes place normally in old age.

Hypertrophy, or **goiter,** is a condition in which there is hyperplasia of the interstitial or glandular tissues. These enlargements are classified under various headings.

Hypertrophy can be divided into two main varieties: (1) *Diffuse* and (2) *nodular.* Both can be subdivided into (*a*) colloid and (*b*) parenchymatous forms.

1. In the *diffuse* variety there is a uniform enlargement, or one lobe may be more enlarged than the other, but it presents no circumscribed nodules differing in structure from the rest of the lobe.

(*a*) Colloid type. In this the follicles are so greatly distended with colloid material that the walls may rupture. The epithelium is flattened and destroyed. The functioning epithelium being destroyed, and the colloid being nonabsorbable, the symptoms of hyperthyroidism do not appear.

(*b*) Parenchymatous type. In this there is a glandular proliferation resembling tumor formation. Solid masses and cords of cells similar to the fetal thyroid are present. Colloid material is lacking or scanty. Papillary projections of epithelium into the acini, papillary cystic goiter, may be found. On account of the increase in functioning tissue the symptoms of hyperthyroidism appear.

2. In the *nodular* variety there are found circumscribed areas surrounded by a connective-tissue capsule. These

areas may show colloid or parenchymatous changes. Both forms may be present in the same thyroid. Fatty as well as hyaline changes are common in the nodes. Between these areas the gland tissue may be normal, degenerated, or atrophic. *Cysts* may arise through the absorption of the walls separating the acini and allowing large accumulations of colloid to form (Fig. 9).

Hyperthyroidism, *Graves'* or *Basedow's* disease, *exophthalmic goiter*, is an enlargement of the gland associated with exophthalmus, palpitation of the heart, tachycardia, tremors of the hands and vasomotor disturbances. The blood-vessels are dilated, interstitial hemorrhages may occur, and these are sometimes followed by necrosis. There is a proliferation of the epithelium of the acini, with a decrease of the colloid material. The symptoms may be due to an excess of iodin formation or of iodin absorption.

The effects of goiter may be *local*, as a result of the pressure exerted, or *distant*, on account of some disturbance of nutrition. Its cause is unknown. In certain countries it is endemic, and more common in high altitudes than in low.

It is very commonly associated with cretinism, occurring in about 60 per cent. of such cases.

Hypothyroidism is a condition in which there is a decrease in the thyroid activity. It may be divided into the following forms:

1. Endemic cretinism. Gland shows areas of atrophy and of goitrous degeneration.

2. Sporadic cretinism, due to congenital absence of the thyroid.

3. Infantile myxedema. Acquired loss of perversion of thyroid function in early life.

4. Adult myxedema. Spontaneous diminution in thyroid tissue, with degeneration of the parenchyma and overgrowth of connective tissue.

5. Operative myxedema (cachexia strumipriva). Due to operative removal of the thyroid.

In *myxedema* there is a marked thickening of the skin, due

partly to a tissue resembling granulation tissue, containing an increased number of fibrils and nuclei; partly to an infiltration by an amorphous material, resembling mucus, in the lymph spaces.

Hyperemia occurs in cardiac disease and when there is obstruction to the circulation by tumors. The gland may in consequence be much enlarged. In Graves' disease the gland is very vascular.

Inflammation (**thyroiditis**) is not common. It may follow traumatism or infection, and varies in its severity. Suppuration may occur with, at times, fatal results. The pus may remain confined within the capsule, and by pressure interfere with respiration. The abscess may perforate the trachea, esophagus, or skin, or it may follow along the cervical fascia into the mediastinum.

Tuberculosis, syphilis, and **actinomycosis** are very unusual, but have been observed.

Tumors.—*Fibromata* in the form of circumscribed nodules occasionally occur.

Sarcoma is a common primary tumor of the gland. It occurs in all forms, the round-cell variety being the commonest.

Carcinoma is the commonest form of primary tumor. It begins usually in an adenomatous goiter, and is of the adenocarcinomatous type. It grows rapidly, soon invades the tissues of the neck, and frequently gives metastases to the lungs, bones of the skull, inferior maxilla, sternum, and the long bones. The metastases may resemble normal thyroid, contain iodin, and may carry on the normal function. Degenerative changes are quite common.

Adenoma can seldom be differentiated from a glandular hyperplasia unless the growth is distinctly circumscribed.

PARATHYROID GLANDS

These are four small, gland-like bodies situated along the posterior inner edges of the lateral lobes of the thyroid gland, usually two on a side. They seem to be of great importance in the metabolism of the body. When removed fatal *tetany*

results. This is characterized by convulsions, spasmodic contractions, rapid and labored respiration and salivation. These may be due to disturbances of the calcium metabolism, or to the presence within the circulation of a toxin that is normally neutralized by the parathyroid activities.

THE ADRENALS

Malformation.—They are seldom absent, but may be unusually small. Supplementary adrenals are not uncommon, and inclosure of fragments in the liver, kidney, and genital organs is quite frequent. They generally consist entirely of tissue of the cortical type. These may give rise to *hypernephromata.*

Fatty degeneration is quite common. The gland is yellowish and soft. The medullary portion mainly is involved, the cortex remaining as a thin wall. On account of postmortem changes taking place so rapidly, it is at times very difficult to accurately judge the importance of the lesion.

Amyloid changes occur in the blood-vessels as a part of general amyloid disease.

Pigmentation is present in senility. The cortex contains fine yellowish granules.

Hemorrhage sometimes occurs either as a result of injury or of constitutional conditions. The blood may be absorbed or encysted, with induration and calcification.

Syphilis occasionally occurs, either as a gumma or an induration.

Tuberculosis of the adrenals is not uncommon. It is frequently a part of a general miliary involvement.

Primary tuberculosis, in the form of a caseous degeneration, is the lesion most generally associated with Addison's disease. The adrenals are enlarged, nodular, and the capsule is thickened. Caseous areas and small cavities filled with a thick, curdy pus are frequently found. Calcification may take place.

Tumors.—*Sarcoma*, *adenoma*, and *carcinoma* may occur as primary growths, and are not infrequently associated

with Addison's disease. As secondary growths they are more common.

Addison's disease is a peculiar condition characterized by a deposit of pigment in the skin in the cells of the rete Malpighii, sometimes in the corium. "This discoloration pervades the whole surface of the body, but is commonly most strongly manifested on the face, neck, superior extremities, penis and scrotum, and in the flexures of the axilla, and around the navel. It may be said to present a dingy or smoky appearance, or various tints or shades of deep amber or chestnut brown."

The condition probably is due to disturbances of an atrophic nature within the chromaffin cells, either in the adrenal or in other portions of the sympathetic system. In those cases in which there is a destruction of the adrenals without the appearance of Addison's disease the chromaffin cells of the organ may be uninvolved or cells of a similar type elsewhere may have taken on a compensatory activity.

In the majority of cases there is tuberculosis of the adrenals, usually of both but sometimes unilateral. It may be primary, but generally is associated with tuberculosis of the lungs, genito-urinary tract or bones. Next in importance is an atrophy due to chronic interstitial connective-tissue formation with contraction. Carcinoma of the adrenals has been noted also in this disease.

CHAPTER XXVI

SPLEEN, LYMPH-NODES, THYMUS, AND BONE-MARROW

THE SPLEEN

Malformations.—Total absence may occur. It may be divided into lobes, and accessory or supernumerary spleens of small size are quite common.

The organ may be unusually movable. It may be much displaced by pressure from neighboring organs or collections of fluids.

Anemia may be part of a general condition or follow severe hemorrhage. The organ is smaller than normal, pale, and the capsule is much wrinkled. On section, the stroma is prominent and the color is a reddish-gray or slate.

Hyperemia.—*Active hyperemia* is physiologic after a large meal, and is almost constantly present in the infectious fevers. The spleen may be several times its normal size, is dark red in color, and the capsule is greatly stretched and the pulp so very soft, almost semifluid, that it oozes from the cut surface. If the condition is acute, the swelling is due to the hyperemia. If long continued, the connective tissue may increase in both the trabeculæ and the capsule.

This active hyperemia is especially common in typhoid fever, and the micro-organisms can usually be recovered from the spleen.

Passive hyperemia is due to obstruction of the circulation, as in cirrhosis of the liver and chronic heart and lung diseases. The condition is known as cyanotic induration, on account of the characteristic color and firmness. The spleen is larger and bluish-red in color; the capsule is tense, and the pulp soft. As the condition persists, there is an increase in the connective-tissue of the capsule and the trabeculæ. There

may be finally an atrophy of the splenic pulp, with contraction of the fibrous tissue, so that the organ becomes smaller, firmer, and somewhat distorted.

Hemorrhage is usually the result of traumatism, and occurs beneath the capsule. It may occur spontaneously in certain forms of disease, as typhoid fever and malaria. A common form is that which occurs in *hemorrhage infarction* as a consequence of embolism. The conic area has its base toward the periphery and the apex toward the hilum. The infarcts may be small or large, single or multiple. It rapidly breaks down, and if micro-organisms are present, an abscess may form. Otherwise the detritus is gradually absorbed and replaced by fibrous tissue which forms an irregular, contracted scar in which there is frequently more or less pigment.

Embolism is quite common and causes either hemorrhagic or anemic infarcts. The anemic is similar to the above, except that it is paler on account of containing less blood.

Thrombosis of the splenic vein is generally secondary to a similar condition of the portal vein.

Splenic tumor is the term applied to the enlargement that occurs in infectious diseases. The spleen may be three to four times the normal bulk, dark colored, red or reddish-black, and very soft; the capsule is stretched; the trabeculæ and the Malpighian bodies are invisible on section, and the tissue is very friable and mushy. Microscopically the vessels are dilated and the pulp is composed of great numbers of lymphocytes and polymorphonuclear leukocytes. Many large mononuclear cells containing erythrocytes are present. Mitotic figures are frequently found in them. Small areas of focal necrosis are also frequently present.

The enlargement of the spleen subsides as the disease declines, but it seldom gets quite as small as before the attack, on account of the fibrous overgrowth that occurs.

Acute splenitis is usually of a suppurative character, due usually to hematogenous infection, in the form of septic emboli. Abscesses, either single or multiple, form. They may be absorbed or may rupture into some neighboring cavity, as the peritoneal, or into the stomach, intestine, lung, or pleura.

Chronic splenitis is generally diffuse, and is characterized by a great hyperplasia of the connective tissue. In its most marked form it occurs in chronic malaria. It may also occur in either congenital or acquired syphilis, in prolonged typhoid fever, and in leukemia and pseudoleukemia.

The spleen is at first enlarged, but becomes smaller as the process continues. The capsule is stretched and much thickened, and may contain circumscribed areas that are almost cartilaginous in their density. The trabeculæ are also thickened. The organ is then quite firm, and may be dark in color on account of the presence of pigment.

Microscopically there is a hyperplasia of both pulp and interstitial tissue.

Perisplenitis is an inflammation of the capsule of the spleen usually resulting in the production of an increased amount of connective tissue. The capsule becomes much thickened over a considerable area and adhesions may form between it and adjacent structures.

Tuberculosis of the spleen is rare as a primary affection, but is quite frequent as a secondary condition, and appears as a miliary infection. The tubercles are small grayish spots, not unlike the Malpighian corpuscles. They undergo a central caseation. At times the tubercles may be as large as a pea but not as numerous as in the miliary type.

Syphilis is very rare, but occurs in the form of gummata. They are generally multiple, and at first grayish, later becoming yellowish on account of degeneration in the central part of the node. There may also be a diffuse increase of the connective tissue.

Atrophy of the spleen is very common in old age. The capsule is wrinkled and thickened, and the organ is pale, flabby, and pigmented, and there is an increase in the stroma. Circumscribed areas in the capsule of extreme thickness and cartilaginous density may be present and be the cause of atrophy.

Degenerations.—*Amyloid* disease affects the spleen more frequently than any other organ. It makes its appearance in the walls of the blood-vessels in the Malpighian bodies,

and involves the adjacent connective-tissue, with atrophy and at times disappearance of the lymphoid cells. The bodies become enlarged, pale, and translucent, resembling boiled sago, hence it is known as the *sago spleen*. Such a spleen is generally about normal in size. Occasionally the degeneration may be more diffuse, affecting the connective-tissue stroma. The organ may be greatly enlarged. The cut sur-

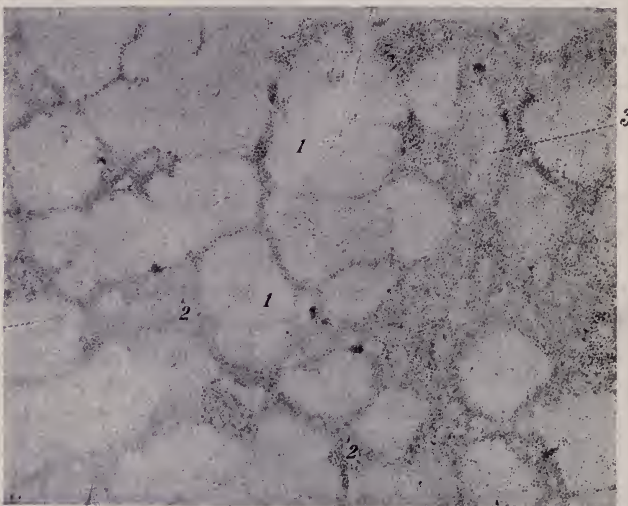

FIG. 181.—AMYLOID DEGENERATION OF THE SPLEEN (SAGO SPLEEN). × 24 (Dürck).

1, An amyloid follicle, in which are seen only a few nuclei; the blood-vessels, in transverse section, have also undergone amyloid degeneration; 2, compressed pulp-spaces; 3, trabeculæ.

face is dry, translucent, firm, and friable, and is about the same color as dried beef. The edges also are rounded. The degenerated areas give a mahogany-brown color on the addition of iodin.

Pigmentation of the spleen is found in chronic congestion, as in cirrhosis of the liver and in malaria. Hemolysis takes place, and the freed pigment is found in the walls of the blood-vessels and in the parenchyma cells. In malaria the pig-

ment is melanin, in other conditions hemosiderin. External pigment, as coal-dust, may lodge in the spleen. It gains entrance into a blood-vessel by erosion from pressure of an anthracotic lymph-node.

Calcification is found occasionally in old infarcts, in a thickened capsule, and in degenerated areas of tuberculosis and syphilis.

Leukemia.—The spleen becomes greatly enlarged, weighing at times as much as 5 to 10 kilograms. The capsule is much thickened. In the early stage the organ is enlarged and soft, but finally becomes firm and dense, on account of the hyperplasia of the lymphoid tissue. On section, the spleen is seen to be very much congested, and the Malpighian bodies appear quite prominent.

There is anemia resulting from pressure of the capsule on the pulp; many of the cells degenerate, and both anemic and hemorrhagic infarcts may occur. On section, the cut surface is found to be very mottled. Reddish areas, small yellowish necrotic masses, whitish bodies of lymphoid tissue, and infarctions may all be present. Microscopically the Malpighian corpuscles are found much enlarged, and contain cells showing mitoses. The new cells may be larger than normal, and giant-cells are occasionally seen. The pulp is congested and degenerated, containing pigment and large phagocytic cells in which are found erythrocytes and detritus.

The changes in lymphoid and myelogenous leukemia are very much alike except that in the latter many myelocytes are present and the spleen is larger.

Tuberculosis is not infrequently present at the same time as leukemia, and may modify the general appearances.

Pseudoleukemia.—The gross appearances are practically the same as in leukemia, but there are differences in the microscopic picture. "In the spleen and lymph-nodes there is hyperplasia of the lymphoid tissue, proliferation of the reticular endothelial cells, formation of uninuclear and multinuclear giant-cells, thickening of the reticulum, and final overgrowth of connective tissue. Eosinophiles, though not

specific, are frequently found in great abundance. There is also an increase in the eosinophilic leukocytes and myelocytes of the bone-marrow."

Splenic Anemia (*Primary Splenomegaly, Banti's Disease*).—The spleen shows a general hyperplasia of connective tissue of varying degree, involving the capsule, the reticulum of the pulp, and in particular the Malpighian bodies. These latter may show hyaline changes. The blood spaces in many cases show more or less hyperplasia of the lining endothelial cells. Sometimes this proliferation may be so extensive as to suggest true tumor formation. (Gaucher type.) Areas of hemorrhage, infarcts, and perisplenic adhesions are occasionally found.

In the terminal stage of splenic anemia the liver may show a more or less marked degree of portal cirrhosis (Banti's disease).

Tumors.—Primary growths are rare. Secondary sarcoma and carcinoma are sometimes found in generalized metastases.

Cysts are rare. Small ones may be due to degeneration of a follicle. Large ones are occasionally found.

Parasites are also rare, but the *Pentastomum denticulatum*, the cysticercus, and the *Tænia echinococcus* have all been described, the last the most frequently.

THE LYMPH-NODES

Anemia.—The nodes are softer, shrunken, and drier than normal.

Hyperemia is characterized by an increase in size of the nodes, which are reddish in color and very moist. The change is more marked in the capsular and cortical portions than in the center. It is generally the beginning stage of inflammation.

Atrophy of the nodes occurs chiefly in old age. The lymphocytes in the medullary portion degenerate, fatty metamorphosis of the connective tissue occurs, and the nodes become smaller, hard, and dry.

Hypertrophy is usually considered among the tumors as *lymphadenoma*.

Degenerations.—*Amyloid* occurs in cases of general amyloid disease. The tissues first affected are the walls of the small blood-vessels and the connective tissue of the trabeculæ; the endothelial cells are affected later.

Hyaline changes are occasionally seen in the walls of the blood-vessels and trabeculæ.

Calcification of lymph-nodes is a not infrequent end result in necrotic lesions. There may be small scattered areas of calcareous matter or a diffuse infiltration of the node.

Pigmentation may result from the presence of internal or external substances. Hemosiderin is the commonest blood-pigment. It may form as a result of local extravasation of blood, or it may be carried to the node by the blood from a hemorrhage in some adjacent tissue. The pigment-granules are found within the lymphocytes or in the cells of the stroma. The amount present may be very scanty, or so plentiful as to give a rusty color to the tissue.

External pigments, as in pneumonokoniosis in or tattooing, may find their way into the lymph-nodes, being carried there by leukocytes and other phagocytic cells. Anthracotic pigmentation is generally well marked in the bronchial lymph nodes. As a rule, the substances acting as irritants bring about a connective-tissue hyperplasia with destruction of the lymphoid tissue. Occasionally softening may result instead. If septic material is conveyed to the nodes, suppuration occurs.

Inflammation or **lymphadenitis** is secondary, as a rule, to the extension of inflammation following infected wounds in neighboring tissues. The infection is commonly of lymphogenic origin. The node becomes swollen, hyperemic, and tender. It may be dark red from hemorrhages. Microscopically the lymph spaces are found filled with erythrocytes, leukocytes, desquamated endothelial cells, and some fibrin. These endothelial cells frequently contain red blood cells, leukocytes, and fragments of other cells.

The process may be so severe as to bring about suppuration and abscess formation. Such a condition in the superficial nodes is termed a *bubo*. If deep-lying nodes are the

seat of abscess formation, serious consequences may result from perforation into some internal cavity.

If the inflammation subsides during the early stage, absorption of the exudate takes place, the leukocytes pass into the circulation or break down, and the fibrin also softens. If there has been pus-formation, absorption may not take place. The pus causes hyperplasia of the neighboring connective-tissue cells, and they form a capsule. Such abscesses may calcify. At times the necrotic masses may be entirely absorbed and be replaced by a great overgrowth of connective tissue.

Chronic lymphadenitis may follow numerous acute attacks or long-continued irritation, as in tuberculosis, syphilis, and other chronic infectious diseases. There is an increase in the connective tissue, with usually atrophy or necrosis of the lymphoid structures. Calcification may follow.

Tuberculosis of the lymph-nodes may be primary, but is much more frequently secondary to disease in a neighboring structure. The specific organism is carried to the node by the lymph-channels.

In tuberculosis of the cervical nodes the tubercle bacillus gains entrance through the tonsil without causing disease at that point. The same condition may occur in the mesenteric nodes without involvement of the intestinal mucous membrane.

The tuberculous nodes are enlarged, and at first hyperemic, although later they become paler. In the substance of the node numerous miliary tubercles may be seen, or the tissue may be represented by a broken-down caseous mass in the center. The caseation may continue until the node becomes a softened semifluid mass. The process may involve neighboring structures, and finally rupture externally, with the formation of a discharging sinus.

If the course is less acute, there may be very extensive connective-tissue hyperplasia around the disease focus, further involvement being thus prevented. Calcification may finally take place.

This variety of tuberculosis is comparatively benign. It must be remembered, however, that although a node becomes

encapsulated and even calcified, it is still infectious. Though the organisms may not be recognizable microscopically, yet injection of the material into animals will usually give rise to the disease.

The microscopic appearances are the same as are found in tuberculosis in other parts of the body.

Syphilis.—The lesions vary according to the stage of the disease. During the primary lesion the adjacent nodes may be the seat of an ordinary acute inflammation. They may become quite swollen and at times undergo suppuration. Such a condition is due probably to there being a mixed infection.

In the secondary stage there is a lymphadenitis in which the nodes are hard, and there is no tendency to soften and suppurate. Microscopically there is seen a round-cell infiltration, with thickening of the trabeculæ and proliferation of the endothelium of the lymph-spaces. The walls of the blood-vessels are thickened, and show round-cell infiltration.

In tertiary syphilis small gummata may form in the lymph-nodes, particularly in the lymph-sinuses. They are grayish, degenerated, and gummy, and are composed of leukocytes, lymphocytes, and other cells, all of which show fatty and hyaline degenerations.

Leprosy, glanders, and **actinomycosis** are present at times in the nodes, and show characteristic lesions.

Tumors.—*Leukemia.*—In the lymphatic form there is a general hyperplasia of the lymphatic tissues in the body. A few nodes or many may be involved, and metastatic deposits of lymphoid cells are found where normally none exist. Little change is evident; under the microscope, the enlargement is seen to result mainly from an increase of the lymph-cells without much hyperplasia of the reticulum or vessels.

The diagnosis has to be made by the changes present in the blood.

Pseudoleukemia (*Hodgkin's*) *disease* is a condition somewhat resembling an infectious disease, and is characterized by certain changes occurring quite generally in the lymphatic tissues but starting as a rule in the cervical and axillary nodes. The appearances as described in the spleen (*q. v.*) are

the same as occur in the lymph-nodes. The blood shows no definite changes.

Lymphoma or *lymphocytoma* refers to all enlargements of the lymph-nodes irrespective of the cause. The general classification includes all those conditions in which the essential change is an overgrowth of lymphocytes occurring primarily in pre-existing lymphoid tissue. May have all transitions from simple hyperplasia to a malignant cellular invasion of the surrounding tissue. The nodes are described as being of two varieties, the hard and the soft.

In the *hard* variety the nodes are enlarged and hard, the capsule thickened, and the trabeculæ increased. There is a great increase in the connective tissue and some hyperplasia of the lymph-cells.

In the *soft* the nodes, though enlarged, are softer and grayish. They do not suppurate. Microscopically the increase of the lymphoid tissue is the marked feature.

The enlargement of the nodes is sometimes referred to as *lymphosarcoma,* particularly when metastatic deposits of lymph-tissue are found in various organs, as the liver, kidneys, and heart.

Sarcoma may develop in a lymph-node, and, breaking through the capsule, involve adjacent tissues. Metastases occur in the internal organs without involving other lymph-nodes, and in that way is differentiated from lymphosarcoma. Microscopically the primary tumors may resemble each other so closely that they frequently cannot be told apart. Other forms than the round-cell, such as spindle-cell, occur.

Carcinoma, secondary in origin, is a very common condition of the lymph-nodes. It is found in those nodes that are nearest to the seat of the disease, and is due to the carrying of carcinomatous cells by the lymph-stream to the node or by a continuous growth along the lymphatics.

THE THYMUS GLAND

Malformations.—The gland may be very small or completely absent. Sometimes it is so much enlarged as to

cover the pericardium and the great vessels. It generally begins to atrophy by about the second year, but traces may remain until puberty or later.

Hypertrophy, mainly of the lymphoid portion, may be present in cases of sudden death. In such instances there are usually lesions of the ductless glands, as thyroid.

Hyperemia with punctate hemorrhages is found in cases of death from asphyxia.

Inflammation is very rare, and takes the form of small abscesses. It may occur from extension of inflammations from adjoining tissues.

Tuberculosis occasionally occurs.

Syphilis occurs in the form of gummata, particularly in the newborn with congenital syphilis.

Tumors.—*Lymphoma* and *lymphosarcoma* may originate within the thymus or its remnants.

THE BONE-MARROW

The marrow is lymphoid tissue consisting of a connective-tissue reticulum in which are numerous capillaries and venous vessels. The marrow-cells are large and round, and contain clear nuclei of vesicular character. Besides these there are many eosinophilic cells, endothelioid cells, fat cells, nucleated and non-nucleated red blood-corpuscles, giant-cells, and cells containing erythrocytes and pigment.

In early life the marrow of the long bones is reddish, but the color finally changes to yellow, on account of the increase of the fat.

Anemia.—In *pernicious anemia* the fatty tissue disappears and the marrow returns to its early condition. The color, normally yellow, becomes a darker red than usual. A few myelocytes and many nucleated red cells are present. The change begins at the epiphyses, and extends toward the center of the shaft.

In *myelogenous leukemia* the marrow is rather gray in color, and scattered throughout may be seen small pale areas which consist mainly of myelocytes. These areas may be so numer-

ous as to give an appearance of suppuration. Numerous nucleated red blood cells are also present. The myelocytes in myelogenous leukemia are supposed to be formed in the bone-marrow.

In *lymphatic leukemia* the changes are slight.

In *typhoid fever* the marrow contains areas composed of many lymphoid cells, large phagocytes, and foci of necrosis. The lesions are similar to those found in the other lymphatic tissues in typhoid.

Atrophy occurs in old age and marasmic conditions. The fat is absorbed, and the number of cells decreases.

Hypertrophy is the term applied to the changes that take place in anemic conditions.

Degenerations.—*Fatty infiltration* occurs normally up to about the sixteenth year. It may be developed excessively in cases of general obesity and in conditions of ill nutrition.

Mucoid degeneration is sometimes seen.

Fatty degeneration occurs in severe infections.

Necrosis may be part of inflammatory conditions.

Pigmentation occurs in the marrow in cases of malaria, or in conditions causing hemolysis. External pigments, as anthracosis, may be deposited in the marrow by the blood.

Inflammation or **osteomyelitis** occurs in the various severe infectious diseases, as typhoid fever, smallpox, etc. The marrow becomes redder than normal, punctate hemorrhages occur, focal necroses and cellular infiltration of the blood-vessel walls are present, and also granular degeneration of the cells. At times the marrow may be distinctly purulent. The specific diseases and tumors are dealt with in the chapter on Diseases of the Bones.

CHAPTER XXVII

DISEASES OF THE BRAIN

THE DURA MATER

Hyperemia may be active as a result of injuries or disease of the skull. Passive hyperemia may follow thrombosis of the venous sinuses. Neither of the above can be well recognized post-mortem, as by that time hypostasis has taken place and the blood has sought the lower levels.

Thrombosis of the sinuses is frequently secondary to extension of inflammation from adjacent bony structures, as in mastoid and middle-ear disease. It also occurs in infectious diseases, and is usually located in the superior longitudinal sinus. Cerebral softening or abscess formation with pulmonary or cardiac embolism may follow thrombosis and cause death.

Hemorrhage is commonly due to injury, and may take place on the internal or external surface of the dura. A comparatively large amount of blood may collect between the skull and the dura—an *internal cephalhematoma*—and give rise to serious compression symptoms. Small hemorrhages, frequently multiple, may be found in the substance of the dura after death by suffocation.

Inflammation of the Dura.—*Acute pachymeningitis* is the result of infection following injury or disease of the skull. It may be local or general, and is characterized by the presence of pus. The dura is much thickened and swollen by round-cell infiltration, and is covered by a layer of purulent material. *Hemorrhagic pachymeningitis* is found in the old, the insane, and in alcoholics, usually in the area that is supplied by the middle meningeal artery. It consists of a chronic inflammation of the internal layer of the dura mater, characterized by the formation of layers of new, delicate con-

nective tissue with numerous very thin-walled blood-vessels from which the blood is prone to escape. At times this may be so extensive as to simulate a hemorrhage. The coloring-matter may be absorbed and leave a collection of serous fluid—a *hygroma*.

In more advanced stages the new membrane may become greatly thickened, its outermost layers being changed into dense fibrous tissue with the obliteration of the vessels.

Chronic internal pachymeningitis is of obscure etiology, probably hematogenic, and is usually accompanied by disease of the pia and arachnoid. It is characterized by the

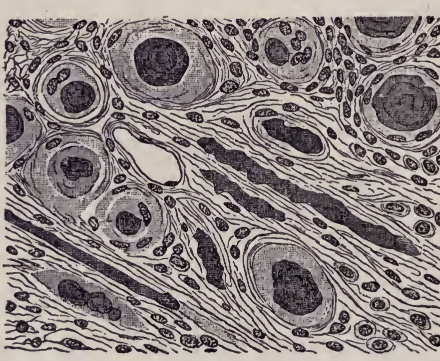

FIG. 182.—SECTION OF A PSAMMOMA OF THE DURA MATER. × 200 (Ziegler).

deposition of numerous layers of fibrinous exudation upon the internal surface of the dura. These gradually undergo fibrous replacement, with frequently the formation of many new capillaries. The dura becomes more adherent to the bone, and calcareous infiltration is sometimes encountered.

Tuberculosis of the dura usually follows tuberculous disease of the bones of the skull or of the pia-arachnoid. It may be present as miliary tubercles or as large caseous masses.

Syphilis may give rise to a *pachymeningitis fibrosa*, causing a dense thickening of the dura. It may also be present as gummata, which may have originated either within the

dura or within the bones of the skull, and have secondarily invaded the membrane.

Tumors.—The most common is the *sarcoma*, which may be either spindle or round-celled, and quite often alveolar. These growths extend from the inner surface of the dura toward the brain. They may be flat or more elevated, and vary greatly in size. If they form on the outer surface of the dura, they may cause absorption of the bone and perforation. If the blood-supply is very rich, these growths are called *angiosarcoma*. *Endothelioma* may develop upon the inner surface of the membrane. Other forms of primary tumors are rare, psammoma, lipoma, and fibroma seldom occurring.

Secondary tumors may follow malignant disease of neighboring structures—may be sarcoma, glioma, or carcinoma.

Parasites are rare; the echinococcus and the *Cysticercus cellulosæ* have been described.

THE PIA AND ARACHNOID

Circulatory Disturbances.—*Anemia* occurs only as a part of a general condition.

Active hyperemia is frequent, being the earliest stage of meningitis. It is also found in death from alcohol, in the infectious fevers, as typhoid and cholera, in certain poisonings, and in delirium of various kinds. The pia is red, and the smaller vessels are injected. The subarachnoid fluid may be increased in amount and cloudy.

Passive hyperemia is rather difficult to recognize postmortem, on account of the hypostasis that occurs. The large veins are distended and tortuous, the arachnoid is cloudy and there may be more fluid than normal. This condition occurs in chronic heart and lung diseases and in venous obstructions.

Hemorrhage into the subarachnoid space from the vessels of the pia may occur in anthrax and in such diseases as scurvy, hemophilia, and in severe infections. The hemorrhages may be numerous and small, or there may be a single large collection of blood between the pia and arachnoid. This

latter form is generally the result of some severe injury, or due to the rupture of an aneurysm. The blood, instead of being upon the surface of the brain, may gain entrance into the ventricles.

Small collections of blood may be absorbed and leave nothing but a small, and slightly yellowish area. If the amount has been large, the pigment may be absorbed and leave a clear, serous fluid.

Edema may be present as an increase of the cerebrospinal fluid. A large collection of fluid between the pia and arachnoid is known as an *external hydrocephalus*. In senile atrophy of the brain there is an accumulation of fluid to fill out the loss of substance—*hydrops ex vacuo*. The edema may be gelatinous in character in paresis and insanity.

Inflammations.—Leptomeningitis or inflammation of the arachnoid and pia may be acute or chronic, and the acute may be classified according to the exudate.

Acute leptomeningitis is an infectious condition due to various organisms. The pneumococcus is the one found in the greatest number of cases, but many varieties have been described. In the epidemic meningitis the *Diplococcus intracellularis meningitidis* of Weichselbaum has been recognized as the cause. The infecting agent gains entrance either as a result of wounds, by way of the lymphatics, or by direct extension.

Serous leptomeningitis consists of round-cell infiltration of the membranes, with hyperemia and the exudation into the subarachnoid space and ventricles of a serous fluid. This may be slightly cloudy from leukocytes that are sometimes present. This form occurs in children in the course of infectious diseases, as scarlet fever and measles; and in adults after sunstroke. It is probably the beginning stage of an infectious inflammation in which the death of the patient has followed before further lesions have had time to develop.

Fibrinopurulent leptomeningitis is probably a later stage of the preceding. In the subarachnoid space there is a collection of pus and fibrin. This may increase until the sulci are marked out as yellowish bands, and eventually the sur-

face of the brain may be covered by this purulent exudate. The process may be confined to local areas, or involve both hemispheres. If at the vertex, it is known as *cortical meningitis;* at the base, as *basilar meningitis.*

The pus may gain entrance into the ventricles, or it may follow along the blood-vessels, particularly the middle meningeal, and involve the cortical substance with degenerative changes in both cells and fibers. Small hemorrhages may be present and discolor the exudate. The termination is usually fatal, but absorption and recovery may take place. There are, however, permanent structural changes, as a rule.

Epidemic cerebrospinal meningitis resembles the above form, except that it has a specific organism, the *Diplococcus intracellularis*, as its cause. It generally starts upon the convexity of the frontal lobes, and extends backward and downward, involving the basal membranes and those of the cord later on. Death may, however, take place so suddenly that distinct changes may not be noticeable. When recovery occurs, a general fibrous thickening of the pia and arachnoid may take place.

The spinal changes may be more marked than those of the brain, the cord being covered by a thick yellowish layer of pus and fibrin. Occasionally the central canal may contain pus.

Chronic leptomeningitis is an inflammation of the pia, usually secondary to diseases of the brain or dura. There is a hyperplasia of connective tissue and round-cell infiltration. The thickening may be so great as to cause compression of the brain-substance or obliteration of venous channels. Large or small areas may be involved, and adhesions between the pia and the dura or the brain may form.

Tuberculous meningitis is more common in children than in adults, and is generally found upon the basilar surface. This location is so frequent that the term basilar meningitis refers to a tuberculous process. This disease may be primary, but is, as a rule, secondary to tuberculosis elsewhere, particularly of the lung.

Upon the pia over the pons, about the optic chiasm, and along the Sylvian artery are found the miliary tubercles, the

characteristic lesions of the process. They may also be noticed in the choroid plexus and the ependyma as a result of extension. The tubercles vary in color from gray to yellow, according to their age.

There is generally some exudate, either serofibrinous or purulent, especially if there has been a mixed infection by the pneumococcus. This may be so thick as to obscure the tubercles.

Most of the tubercles are found around blood-vessels, and consist at first of a cellular infiltration, with some thickening of the vessel-wall. Giant-cells are not as common as in tuberculosis elsewhere. As the disease persists, degeneration and caseation take place.

If the infection has been primary, there may be a single large tuberculous area—a *tyroma.* Such a mass may be soft from liquefaction necrosis, or fairly firm; occasionally it may be the seat of calcareous infiltration.

Syphilis is found in the pia, usually in the form of gummata which may extend and involve the brain or the dura. This form is found as circumscribed, flattened thickenings that generally show necrotic processes.

Another form is characterized by a perivascular round-cell infiltration which may become diffuse. This portion of the pia may become quite thickened and grayish-red in color. Caseation takes place around the edge of the node, and the destroyed portion is gradually replaced by dense cicatricial tissue.

It may occur as a widespread leptomeningitis.

Tumors.—The Pacchionian bodies are numerous small, rounded, projecting structures found along the longitudinal sinus. They consist of fibrous tissue that originates within the arachnoid, but as they grow they force their way at times through the dura and cause a firm union of the membranes. There is also very frequently more or less atrophy of the skull, causing depressions into which these bodies fit. In places the bone may be greatly reduced in thickness. These bodies are found in nearly every adult body, and appear to be of no significance.

Endothelioma and *perithelioma* are found in the membranes, having originated from the cells of either the lymphatics or the blood-vessels. They may become sufficiently large to cause pressure symptoms, but are usually small. *Sarcoma* may occur in the form of angiosarcoma or cylindroma. *Fibroma*, *lipoma*, and *myxoma* are occasionally seen. *Cholesteatomata* are sometimes found in the pia, generally at the base of the brain. *Teratomata* are rarely encountered. Secondary growths are not infrequent, either by direct extension or by metastasis.

Cysts are rare.

Parasites are unusual, but the echinococcus and the *Cysticercus cellulosæ* have been observed.

THE BRAIN

Malformations of the brain may be associated with deformities of the skull, or may occur independently. *Acrania* is an absence of the skull, but usually with preservation of the membranes and a small mass of nerve tissue. *Hemicrania* is an undeveloped condition of the skull and brain on one side. *Anencephaly* refers to a condition in which there is almost complete lack of brain-substance; it is usually associated with acrania. *Cephalocele* is a hernia of the brain-substance through fissures or openings.

Hypoplasia or *microcephaly* is a condition in which the brain is unusually small, but properly proportioned. It is frequently associated with some degree of external hydrocephalus. *Macrocephaly*, or increase in size of the brain, is generally due to a hyperplasia of the neurogliar tissue. *Porencephaly* refers to the presence of definite holes or depressions in the brain-substance. It may be the result of softening following infarction.

Hydrocephalus is a collection of fluid either within the ventricles of the brain or in the subarachnoid space. It may be *external* to the arachnoid, or *internal*, and may be *congenital* or *acquired.*

External hydrocephalus is frequently *exvacuo* to supply by an exudate a loss of cerebral tissue.

Internal hydrocephalus is a collection of fluid within the third and lateral ventricles of the brain. The amount of fluid may vary greatly. The process generally begins before birth, and may cause serious obstruction to labor. The condition is generally bilateral. After birth, if the accumulation of fluid persists, there is a very typical deformity of the skull. The presence of the fluid within prevents the bones of the brain from uniting. The sutures are pushed far apart, giving a peculiar bulging to the forehead. The head becomes quite large and round, the face small, and the eyes may project. The cerebral tissue, on account of the pressure, shows a marked flattening of the convolutions.

Fig. 183.—Congenital Internal Hydrocephalus, with Marked Atrophy of the White Substance (from Bollinger).

The dura and pia may be thin or thick, and the choroid plexuses of the ventricles may be hypertrophied or cystic.

The collection of fluid will or will not interfere with the mentality of the individual according to the amount that is present. In very marked cases it is incompatible with life, but, if less severe, the individual may live, although more or less of an imbecile.

The cause of this condition is not known, but by some it is thought to be due to alcoholism in the parents; to inflammatory conditions of ependyma and choroid plexus; to closure of the transverse fissure, causing obstruction to the escape of fluid from the ventricles; and to changes in the pressure within the cerebral veins.

Acute acquired hydrocephalus is generally found as a result

of basilar meningitis. The brain is pale, soft, and the convolutions flattened; the contained fluid is frequently gelatinous. The ependyma and choroid plexuses are injected, and if the process was tubercular, tubercles will be found. The substance of the brain will show under the microscope the presence of small areas of suppuration.

Chronic acquired hydrocephalus generally occurs late in the course of epidemic meningitis or as a consequence of a chronic granular ependymitis.

Ependymitis may be either acute or chronic. The acute form is associated with acute meningitis, and in it there is a thickening and leukocytic infiltration of the ependyma and pia. In chronic ependymitis the surface is granular, the ependyma is thrown into folds and becomes much thicker on account of a hyperplasia of the contained neurogliar fibers.

Circulatory Disturbances.—*Anemia* of the brain is characterized by a pallor of the cortex and white substance as a result of the diminished amount of blood. It is due to general anemia, severe hemorrhage, disease of the blood-vessels, particularly atheroma, increased intercranial pressure, or to spasmodic contraction of the blood-vessels.

Acute Hyperemia.—The amount of blood in the brain is increased during its activity. Pathologically, it is found in beginning inflammations, in infectious diseases, acute delirium, sunstroke, etc. The blood-vessels in the pia are injected, the cortex is darker than normal, and minute hemorrhages may be present.

Passive hyperemia occurs in any of the conditions that prevent the blood escaping from the cerebral veins, as heart disease or local growths. The veins of the membranes are much distended, and the cortex and medulla are of a bluish tinge.

Edema of the brain is generally secondary to conditions causing passive congestion. There may be a slight edema that is soon taken up by the lymphatics. The fluid is most marked in the subarachnoid and ventricular spaces. The membranes are elevated, and the convolutions are flattened. The edematous fluid contains more albumin and is more

cloudy than the normal. Indications of inflammation are usually present. This condition may be a terminal phenomenon. It is found in renal disease and in alcoholism. In the latter there is frequently a great excess of the fluid. Microscopically, there may be some proliferation of the endothelium, and around the blood-vessels there is some round-cell infiltration. Local edema is sometimes found in the neighborhood of areas of softening. In acute hydrocephalus the internal capsules may be involved and transient hemiplegia follow.

Hemorrhage occurs in two forms, *minute* (*punctate*) or *massive.*

Punctate hemorrhages are small collections of blood formed by diapedesis of the erythrocytes or by rupture of a small vessel, due to fatty degeneration of its walls. They are generally found in the cortex, and occur in the course of inflammation of the brain, in various infectious diseases, and in toxic conditions, particularly lead-poisoning. They seldom cause any secondary disturbances.

Massive hemorrhages, unless traumatic, are commonly found to affect the branches of the middle cerebral artery. In these cases there has generally been a pre-existing disease of the vessel, the rupture usually taking place in a small aneurysm. It is commonly known as *apoplexy.* The internal capsule is almost always involved. The pons is quite frequently the seat of hemorrhage, and occasionally the cerebellum, but very rarely the medulla.

The size of the involved area depends upon the amount of blood extravasated and upon the density of the tissue. It is more diffused in the white than in the gray matter. The effects of the hemorrhage may be primary or secondary.

Primary effects are tearing and compression of the brain-substance. If the patient does not immediately die, softening occurs. As a result of the staining by the retained hemoglobin the area is known as red softening. Shortly after the blood escapes it undergoes coagulation, forming a cerebral hematoma. This acts as a foreign body and sets up an inflammatory reaction, with more or less hyperplasia of the

surrounding neuroglia. The fluid portion finally becomes absorbed, the corpuscles broken down, and the pigment liberated, which stains the walls of the cavity. Occasionally a cyst filled with a clear fluid may form. If all fluids are absorbed, the walls of the cavity may come in contact and a scar result.

Other primary effects are distant ones in the form of paralysis, both motor and sensory, and generally on the side of the body opposite to the seat of the hemorrhage. Although there may be a considerable return of the lost faculties, yet in a majority of cases permanent damage is done. This is due to the secondary effects—the *secondary degenerations.* These are systemic, and follow the direction of the nerve impulses. The commonest degeneration is one of the pyramidal tracts. The optic tract and fibers from the temporosphenoidal area may also be involved. In the brain there is finally loss of nerve-cells, without destruction of the neurogliar fibers.

As a result of traumatism, hemorrhages may take place in any part of the brain, with or without fracture of the skull. The hemorrhage may be found on the side of the head opposite to that where the blow was received.

Thrombosis and Embolism.—*Thrombosis* is most common as a result of embolism or of endarteritis. It may be found anywhere, but is probably more frequent in the basilar artery. From obstruction to the nutrition *encephalomalacia*, or softening of the brain, ensues.

Embolism commonly results from a breaking off of a part of a verrucosity or of a leaflet of one of the heart valves, especially the aortic. The greater number of the emboli pass along and finally lodge in the artery of the Sylvian fissure. If the embolus is so large as to remain at the beginning of the artery, there will be a large degenerated area. The corpus striatum, a large part of the internal capsule, and the anterior part of the optic thalamus will be involved. As different branches are obstructed, the areas of degeneration will vary. If the emboli are so small as to enter the posterior perforated space, the optic thalamus only will show small areas of degeneration.

Degenerations.—*Encephalomalacia*, or local softening of the brain, is found in ischemia, as a result of arteriosclerosis of the smaller vessels, in thrombosis and embolism, and in meningitis and encephalitis. The brain-substance breaks down and undergoes colliquation necrosis. The areas of softening are usually referred to by the color that they present. They are, however, not different processes, but merely different stages of the same condition.

White softening is a colliquation necrosis occurring when the blood-supply has been completely and permanently cut off. If this area is incised, the contents will escape, leaving an irregular cavity with ragged borders, and in it will be found some nerve-fibers and neuroglia. The escaped contents are composed of degenerated nerve-structures, with fat-droplets, granule-cells, and leukocytes.

Yellow softening may be due to an increased fatty degeneration occurring in white softening or a late stage of red softening.

Red softening is a breaking-down of nerve tissue accompanied by the extravasation of blood. It may be due to a hemorrhagic infarction or to diapedesis. The contents of the involved area are not generally as fluid as in the other forms of softening.

The areas of softening may vary greatly in size and in the time of their formation. The same process, however goes on, the myelin sheaths degenerate, the axis-cylinders may disappear, compound granule-cells appear, and finally the neurogliar fibers may soften. The broken-down tissue may be slowly absorbed, leaving a cyst with smooth, well-defined walls, and clear contents. The cysts may become encapsulated, or through absorption scar tissue form.

Encephalitis, or inflammation of the brain-substance, is peculiar on account of the tissue that is involved. It differs from inflammation elsewhere in that conditions of degeneration or softening are associated.

Encephalitis may be acute or chronic, diffuse or circumscribed. The causes of the condition are many. It may result from *injury without infection;* in this form there is a

hemorrhagic extravasation, followed rapidly by necrosis. Around the necrotic tissue is a hyperemic zone in which there is some transmigration of leukocytes, and slight proliferation of the connective tissue of the sheaths surrounding the vessels. *Injury with infection* generally affects the membranes primarily, but soon involves the brain-substance. There is a marked leukocytic infiltration along the blood-vessels, and the brain-substance undergoes degenerative processes. Inflammation of the brain may also be secondary to infectious disease elsewhere in the body. In *hematogenic focal encephalitis* specific micro-organisms are brought to the brain by the blood. Numerous areas are found in which the blood-vessels are distended and interstitial hemorrhages are present. The lymphatics contain many leukocytes, and the nerve-tissues rapidly degenerate. If the patient survives long enough, *suppurative encephalitis* may ensue. This form is generally due to infection by the pneumococcus, streptococcus, or staphylococcus, and true abscesses, either single or multiple, are formed. If the extension has been by the blood, they will be multiple; if by direct continuity, as from middle-ear disease, they will be single. The size may vary greatly—they are generally about as large as a walnut. They are most frequent in the cerebrum, but may be found in the cerebellum and rarely in the pons and medulla. When the acute processes subside, a proliferation of the surrounding neurogliar tissue may occur and encapsulate the abscess. *Toxic encephalitis* is caused by the presence, in the circulating blood, of certain substances that act upon the nerve-cells and cause various changes that can be recognized by the employment of special methods of study. These changes are found in the cells of both the brain and spinal cord in diphtheria, tetanus, lead-poisoning, and hydrophobia, also to some extent in alcoholism. *Chronic encephalitis* or *sclerosis* occurs in all cases of injury to the brain in which recovery occurs. There is a chronic hyperplasia of the neuroglia, which may be local or diffuse. In *multiple localized sclerosis* there are numerous scattered foci of degeneration, associated with hyperplasia of the neuroglia. They are sharply defined,

slightly dense to the touch, and grayish or pinkish in color. *Diffuse sclerosis* is characterized by widespread areas of neurogliar hyperplasia. It is more common in children, and does not seem to be due to toxic or inflammatory conditions. It may be sharply circumscribed and resemble glioma. At first the brain may appear hypertrophied, but later, as atrophy of the nerves occurs, it becomes smaller. Certain lobes or convolutions may be involved, and there is always considerable degeneration of the nervous structures.

Tuberculosis of the brain may be primary or be secondary to tuberculosis of the meninges. When secondary, there are generally many small tubercles along the perivascular tissues, particularly along the small vessels of the anterior and posterior perforated spaces. Primary tuberculosis is hematogenic, and occurs as single lesions. It is more common in children. The tubercle gradually becomes larger, and caseous degeneration occurs, is rather dense, yellowish in color, and dry, and sometimes undergoes calcification or again contains a yellowish purulent-like matter. The growth increases in size by the formation and aggregation of new tubercles at the periphery of the original focus. These large areas are called *tyromata*.

Syphilis of the brain generally appears as a gumma that has originated within the pia and extended to the brain. The gumma is at first grayish or reddish-gray, but very soon undergoes a secondary necrosis and caseation. Recovery takes place with the formation of a dense cicatrix. Syphilitic endarteritis is sometimes found and gives rise to secondary degenerations with softening.

Tumors of the Brain.—The most frequent form of those found is the *glioma*. It is commonly found in the cerebrum, the cerebellum, the pons, and medulla. It is thought to never originate from the pia. The glioma appears as a diffuse, poorly defined area, pinkish or reddish in color from the numerous blood-vessels that are present. The tumor may be composed purely of neurogliar tissue, without any nerve-cells or fibers present. Occasionally ganglionic cells, isolated or in groups, are found embedded in the neoplasm; such

tumors are known as *gangliomata* or *neurogliomata*. Microscopically gliomata are made up of cells from which numerous filaments project and which compose the groundworks of the tumor.

Some gliomata are considered as sarcoma, but as the tumors arise from different embryonal layers, such a combination could hardly occur. The sarcoma differs clinically from the ordinary glioma in being of a more rapid growth and giving metastases.

Sarcoma is fairly frequent, and commonly arises from the pia or from the connective tissue around the blood-vessels. It is generally rather circumscribed, and may be encapsulated. The commonest variety is the small round-cell, but spindle-cell and giant-cell forms occur. *Angiosarcoma* is not infrequent, and the *perithelioma* or *myxangiosarcoma tubulare* is fairly common. *Psammosarcoma*, in which infiltration of lime-salts takes place, is occasionally encountered. It is generally small and gritty. *Endothelioma* is found in the pia and sometimes in the choroid plexuses.

Other forms of primary tumors are rare. As secondary growths, sarcoma and carcinoma are fairly frequent.

Parasites are rare; the echinococcus and the *cysticercus cellulosæ* have been found.

THE PITUITARY BODY

Hypertrophy is uncommon, but it occurs in cretinism, myxedema, and acromegaly. If the thyroid gland is removed it is thought that the pituitary body sometimes enlarges. The acini may contain a large amount of colloid material.

Hyperemia may occur, and in cases of passive congestion there may be considerable edema. *Hemorrhage* may take place just before death, and erythrocytes will be found in the connective tissue.

Inflammation is rarely primary, is usually secondary, as a result of extension, and suppuration may occur. The dura covering the gland may become much thickened, and as a result the pituitary body atrophies or undergoes a fibrous change.

Tuberculosis in the form of miliary foci and *syphilis* in the form of gummata have been observed.

Tumors.—*Sarcomata*, round-cell or spindle-cell, are sometimes found. They develop apparently from the capsule of the gland and destroy the substance. They seldom infiltrate the surrounding tissue and do not give metastases.

Adenoma causes a general enlargement and is the growth most commonly found associated with acromegaly. It consists of long, tortuous tubes, and causes atrophy of the posterior or nervous lobe.

Teratoid growths have been described.

Cysts are generally the result of retention of the colloid material. The epithelial cells disappear and the follicles distend. The cysts may grow to the size of a hen's egg.

CHAPTER XXVIII

DISEASES OF THE SPINAL CORD

Circulatory Disturbances.—*Anemia* of the cord may be due to pressure from neoplasms or to obstruction of small blood-vessels by disease or thrombosis. Embolism is followed by necrosis. In pernicious anemia degenerative changes in the posterior columns of the cord may occur.

Hyperemia is present in all inflammations of the meninges or cord. *Passive hyperemia* is present in chronic heart and lung disease. Antemortem congestion is difficult to differentiate, as there is nearly always hypostasis of the blood into the spinal vessels.

Hemorrhage into the cord is less common than in the brain. It may be punctate or massive. The punctate form occurs in death from convulsions, as in tetanus, after injuries, in degenerated areas, about tumors, after extreme congestion, and in other conditions. Massive hemorrhages are seldom larger than a small marble. They may find a way along the longitudinal fibers or occasionally rupture into the central canal.

The changes that take place if the individual lives are similar to those occurring in the brain under like conditions.

Myelitis, although strictly signifying an inflammation of the spinal substance, is used to indicate any form of degeneration present in the cord. It may be primary or secondary. The *primary* form occurs at the seat of the injury, and is frequently a circumscribed condition. *Secondary* degeneration depends upon primary changes elsewhere, and is due to the destruction of nerve-cells or axis-cylinders. It is generally considerably more extensive than a primary degeneration. The degenerated areas may be white, red, or yellow, according to the amount of blood present and the stage of the soft-

ening. In the early stages the involved tissue is swollen and pinkish, and minute hemorrhages may be present. The tissue is at first softened, but finally becomes firmer as fibrous changes occur. Microscopically the myelin is found to be destroyed, breaking down into droplets that stain with osmic acid. The axis-cylinders swell up and degenerate, the nerve-cells show enlargement and finally disappearance of their nuclei. The tissues generally become disorganized and give rise to *white softening*, there being no change in color. If the damage to the cord has been such as to cause extravasation of blood into the involved area, it will be known as *red softening.* As the blood is destroyed the pigment is set free, with the formation of areas of *yellow softening.*

In *purulent myelitis* there will be found a round-cell infiltration in the perivascular spaces, pus in the pia mater, and degeneration of the neighboring nerve-tissues. The ganglion-cells, though very resistant, sooner or later show degenerations.

When the acute processes subside, there is some absorption of the broken-down tissues and a hyperplasia of the neuroglia and connective tissue, constituting the early stage of *sclerosis.* The newly formed tissue is grayish in color, firm, dense, and dry. There is probably little, if any, attempt toward the regeneration of the nerve-fibers.

Myelitis may be traumatic, infectious, toxic, or nutritional.

Traumatic myelitis may result rapidly, but it is usually slow, as a result of compression of the cord by tumors or collections of fluid in the spinal canal. The degeneration generally extends entirely across the cord, being known as *transverse myelitis.* There are usually three stages, that of red softening, of yellow softening, and of gray degeneration, and connective-tissue hyperplasia.

Infectious myelitis may be transverse or disseminated, particularly the latter. Micro-organisms are generally present in the lesions.

Varieties of Myelitis.—When the spinal membranes are inflamed, the condition is known as *spinal meningitis;* if the membranes and cord are both affected, *meningomyelitis.*

Inflammation of the cord alone is known as *myelitis;* disease of the white substance is *leukomyelitis;* if the gray matter, *poliomyelitis.*

Myelitis is referred to as *central* when arising from disease of the central canal; *diffuse*, if it involves the entire cord; *transverse*, when a small section is entirely affected; *disseminated*, when there are numerous small areas more or less widely separated.

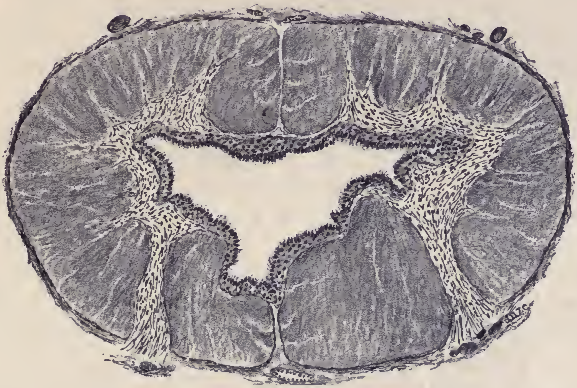

FIG. 184.—HYDROMYELIA (PARTLY DIAGRAMMATIC) (Stengel).

It may be *simple*, *hemorrhagic*, or *purulent*, or, according to development, *acute* or *chronic*.

Hydromyelia is a condition in which the central canal of the spinal cord is dilated by an increased amount of cerebrospinal fluid. The dilatation may be irregular, usually being more marked in the lumbar cord. The canal may be round, slit-like, or triangular, and is commonly lined by ependymal cells, a condition that does not exist normally. Sometimes the canal may be double or even triple, this being more frequent in the lumbar region. *Hematomyelia* refers to the presence of blood in the central canal; *pyomyelia*, when pus is present.

Syringomyelia is characterized by a central dilatation of the spinal canal resulting from the proliferation of the glia about the central canal and subsequent degeneration of the newly found tissue.

The appearance is somewhat similar to that in hydromyelia, but the canal is not lined by ependymal cells.

The etiology of the condition is unknown. There is an extensive proliferation of gliar tissue around the central canal, probably beginning in the cervical portion, but extending down the cord. This tissue rapidly degenerates and liquefies. The cavity is generally posterior to the center of the cord, and may be so large as to leave merely a thin layer of nerve tissue surrounding it. The canal in the early stages is filled with a brownish, gelatinous mass, which eventually undergoes liquefaction, leaving the canal filled with clear fluid.

The extent of the secondary degeneration in the spinal cord and in the anterior and posterior nerve-roots will depend upon the size of the lesion and the amount of pressure exerted. Entire columns of the cord and anterior and posterior nerve-roots may be destroyed in severe cases.

Tuberculosis of the cord commonly involves the meninges, and secondarily extends into the nervous tissues; it is a *meningomyelitis*. Tubercles are present in varying numbers, and soon cause thickenings and necrosis. Disseminated tubercles may be seen in both the white and the gray matter, but are usually microscopic. Primary tuberculosis may occur in the form of a single circumscribed caseous mass.

Syphilis of the cord usually appears as a thickening of the membranes, especially of the dura. Involvement of the pia and arachnoid is uncommon. There is found a marked endarteritis, and the formation of thrombi is quite frequent. Areas of cheesy degeneration are due to the breaking-down of the diseased tissue.

Tumors of the Cord.—The most common form is the *glioma*, as occurring in syringomyelia. It infiltrates the nerve tissue along the posterior portion of the cord. It seldom occurs as a circumscribed growth. *Sarcoma*, *cylindroma*, and *fibroma* are very rare, but have been observed.

Tumors of the spinal meninges are more common. Practically all varieties have been found.

Cysts are extremely rare, but both the echinococcus and the cysticercus have been reported.

Spinal Meningitis.—*Pachymeningitis*, or acute inflammation of the spinal dura mater, is commonly due to neighboring inflammations or to traumatism. In *external pachymeningitis* there is an exudate, cellular or fibrinous, upon the external surface. Abscesses may form and destroy by pressure the neighboring cord. *Internal pachymeningitis* is generally secondary to tuberculous or syphilitic disease of the pia and the bones. There is a marked fibrous exudate, with adhesions between the dura and the underlying membranes. *Hemorrhagic pachymeningitis* is internal, and is similar to the process occurring in the brain. It is characterized by a reddish layer of granulations in which many of the capillaries have ruptured.

Chronic hypertrophic cervical pachymeningitis is a localized thickening of the dura mater in the cervical region. The pia and the arachnoid are also involved. Compression of the cord and secondary degenerations may ensue.

Leptomeningitis, or acute inflammation of the spinal pia and arachnoid, is generally secondary to cerebral meningitis, especially in the epidemic cerebrospinal form. It may be due to local injury or diseases of the bone. There is an exudation, serous, fibrinous, or purulent, upon the inner surface of the dura and the subarachnoid space. The inflammation may be local or involve the greater length of the cord. The tissue of the cord is commonly affected, and extensive round-cell infiltration occurs in the anterior commissure and in the perivascular connective tissue.

SPECIAL DISEASES OF THE SPINAL CORD

Disseminated or **multiple sclerosis** occurs in both the brain and the spinal cord, and is characterized in the early stage by the presence of many softened areas. These vary in size, are grayish in color, are more frequently found in the white matter than in the gray. There is a degeneration of the myelin and of the cells, but the axis-cylinders remain uninvolved for a long time. Hyaline degeneration of the

blood-vessels is commonly present. As the disease progresses, the softened areas are gradually replaced by a hyperplasia of the glia tissue. There is also atrophy of the nerve-cells and of some of the axis-cylinders.

The etiology of this disease is obscure. It is found in syphilis, in acute infectious diseases, in chronic metallic poisoning, and in injuries.

FIG. 185.—TABES DORSALIS (Collins).

Posterior sclerosis, tabes dorsalis, or **locomotor ataxia,** is a condition of sclerotic changes in the posterior sensory columns. The present opinion is that it is the result of primary disease of the posterior nerve-roots. This is thought by many to depend generally upon syphilitic infection, but it occurs in traumatism and possibly in some of the infectious fevers. The lumbar portion is more commonly affected than the dorsal, and lastly the cervical. The degeneration usually develops in the lumbar cord, in the posterior nerve-roots. In the dorsal region there are also two areas of degeneration in the column

of Burdach; and in the cervical region, the chief involvement is in the columns of Goll.

There is atrophy of the nervous tissue, with increase of the neuroglia. The myelin sheaths break down and expose the axis-cylinders, which resist the degenerative processes longer than the other tissues.

In advanced cases there may be almost no normal nerve fibers in the posterior columns, they having been replaced by dense fibrous tissue.

The lesions may not only affect the cord and peripheral nerves, but also involve areas in the brain and in the optic, oculomotor, and trigeminal nerves.

There are also degenerations nearly always present of the sensory nerve-endings.

The main symptoms are girdle pains, loss of knee-jerk, Argyll-Robertson pupils, loss of sensation and tactile sense.

Friedreich's disease, or **hereditary ataxia,** is a variety of posterior sclerosis that usually begins about the seventh year, and involves several members of a family. There is a hypoplasia of the cord or the cerebellum, and sclerosis of the posterior columns of the cord. The fibers in the column of Goll and the greater part of those in the column of Burdach degenerate, and the cells in the column of Clark are involved at times. There is also some degeneration of the direct cerebellar tract and of the lateral pyramidal columns as well. The lesions are most marked in the lower part of the cord.

Acute anterior poliomyelitis is characterized by degeneration and sclerosis of the anterior horns of the gray matter of the spinal cord. It occurs chiefly in children about three years old, but at times affects adults.

The cause is unknown, but the process is that of an acute inflammation. It is apparently either infectious or toxic in its origin and is distributed by the blood-vessels. The disease usually begins rapidly, and is accompanied by chills and fever.

The lesions may be unilateral or bilateral, and are more common in the lumbar region. Early in the disease the blood-vessels of the anterior horns of the gray matter are

distended, and the perivascular lymph-spaces filled with round-cells. Small interstitial hemorrhages may be present in the anterior horns. The ganglion-cells become larger, granular, and cloudy, often vacuolated, and altered in their staining reactions. The cells eventually become completely degenerated and disappear, the medullated nerves lose their covering, and many are destroyed. Neurogliar hyperplasia

Fig. 186.—Chronic Anterior Poliomyelitis (Collins).

occurs in the involved areas, and the gray matter may become much indurated.

Chronic anterior poliomyelitis or **progressive muscular atrophy** occurs generally in adults, and is characterized by atrophy and disappearance of the motor cells of the anterior horns of the spinal cord. The small muscles of the hand are the first to undergo atrophy, then those of the arms, shoulders, and body.

The diaphragm may become involved and death result. The change is one of fatty degeneration.

The lesions generally appear in the cervical and upper dorsal portions of the cord, and extend along the anterior cornua in both directions. When the medulla is affected, the resulting condition is known as *bulbar palsy*.

Bulbar palsy is similar to the above except that it occurs in the medulla instead of in the cord, and affects the ganglia of the hypoglossus, glossopharyngeal, spinal accessory, vagus, facial, abducens, and motor portion of the trigeminus.

Amyotrophic lateral sclerosis is a disease in which there is a degeneration of the peripheral motor nerves as well as an atrophy of the motor cells in the anterior horns of the gray matter of the cord. There is also more or less degeneration of the pyramidal columns. The muscles undergo the same changes as in progressive muscular atrophy.

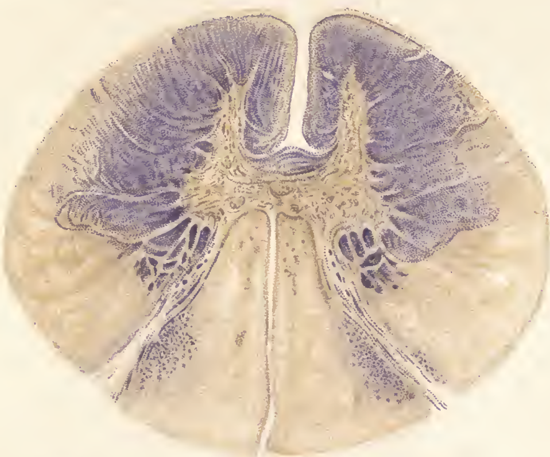

Fig. 187.—Combined Posterior and Lateral Sclerosis (Collins).

The degenerations begin in the sacral and lumbar portions of the cord and extend upward.

Secondary Degenerations of the Spinal Cord.—The microscopic changes are those that have already been described. The degenerations result from lesions in the brain or cord, and when in the cord are described as either ascending or descending, according to the tracts affected.

Descending degeneration is the usual result of disease of the cerebral cortex and internal capsule. It involves the motor tracts and the anterior and lateral pyramidal columns.

If the lesion is unilateral and above the decussation, the anterior tract on the same side and the lateral pyramidal tract on the opposite side will be affected.

Ascending degeneration usually follows transverse myelitis and involves the sensory tract, the posterior columns below, and the columns of Goll above.

THE PERIPHERAL NERVES

Atrophy may result from pressure, from inflammation, or from an interruption in the continuity of the nerve. The myelin sheaths undergo degeneration, and later on the axis-cylinders break down.

Degeneration of the nerves is with difficulty separated from inflammation. When non-inflammatory, is a *simple* degeneration; otherwise an *inflammatory* degeneration. The inflammatory ones are known as *parenchymatous* neuritis, in contradistinction to the *interstitial*, which involve the nerve-sheaths.

Degeneration is found in injuries, in infectious diseases, and in intoxications. Certain nerves or sets of nerves may be involved in the different conditions, as those of the pharynx in diphtheria, those supplying the extensor muscles of the forearm in lead-poisoning, or the cord in syphilis.

The degenerative changes may appear within twenty-four hours after an injury. The myelin sheaths become granular and cloudy, and finally break down into droplets. Larger drops form, fatty degeneration occurs, and leukocytes make their appearance. The axis-cylinders resist for a longer time, but they become nodular, vacuolated, and break up. The degeneration occurs more rapidly in the distal than in the proximal end. Regeneration may take place, but the nerve is usually replaced by a cord of fibrous tissue.

Neuritis.—The so-called *parenchymatous* neuritis is a degeneraton of the nerve-fibers without involvement of the connective tissue. *Interstitial* neuritis is a true inflammatory process affecting the connective tissue.

Acute interstitial neuritis is due to the same causes as bring

about the degenerations. It is characterized by an exudation into the endoneurium and perineurium. There are edema and congestion, with an infiltration of round-cells and at times pus-cells. At the same time there is commonly degeneration of the nerve-fibers. The nerves are swollen and reddened.

Chronic neuritis is interstitial and follows an acute attack, or is due to various infections and intoxications, as chronic lead- or alcohol-poisoning. There is a marked hyperplasia of the connective tissue, with associated degeneration and atrophy of the nerve-fibers.

Tuberculosis of the nerves is due to secondary involvement through extension. The roots of the nerves are generally affected. There are a hyperplasia of the connective tissue and a secondary degeneration of the nerve-fibers.

Syphilis of the nerves occurs commonly in the nerve-roots. It is characterized by a round-cell infiltration at first, and later by a marked hyperplasia of connective tissue, associated with atrophy and degeneration. Gummata have been observed in the cranial nerves.

Leprosy of the nerves is characterized by nodular lesions along their course. There is a proliferation of the bacilli, with the formation of nodes in the fibers, accompanied by cellular infiltration with connective-tissue hyperplasia and degenerations. The lepra bacilli can be found within the tissues.

Tumors.—*Neuromata* are the most frequent form of them, the *false neuroma*, which is more common than the true, is a growth taking place within the connective tissue of the nerve; it is similar to a fibroma.

Sarcomata occur, but are rare.

The malignant tumors may occur as secondary growths.

INDEX

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